Evidenztabellen für die Version 1 der S3-Leitlinie Speicheldrüsentumoren des Kopfes

Version 1.0 – Juli 2025

AWMF-Registernummer der Leitlinie: 007-102OL

Inhaltsverzeichnis

1.1 Sammlung 01a. Welche diagnostischen Verfahren sind bei der Identifikation von Raumforderungen der Speicheldrüsen effektiv? Excision vs. Biopsy

OXFORD (2011) Appraisal Sheet: Systematic Reviews

Liu, C. C. et al. Sensitivity, Specificity, and Posttest Probability of Parotid Fine-Needle Aspiration: A Systematic Review and Meta-analysis. Otolaryngol Head Neck Surg. 154. 9-23. 2016				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 3 Study type: Systematic review and meta-analysis of diagnostic studies (70 studies). To analyze the sensitivity and specificity of fine-needle aspiration (FNA) in distinguishing benign from malignant parotid disease. To determine the anticipated posttest probability of malignancy and probability of non-diagnostic and indeterminate cytology with parotid FNA. Databases: PubMed and Embase Search period: (January 1, 1964, to November 1, 2014). Inclusion Criteria: 1. the study	Population: Adults and/or children presenting with clinically or radiographically identified parotid masses who subsequently underwent parotidectomy. Intervention: FNA was performed prior to surgery via palpation or ultrasound guidance. Comparison: Cytopathology results from the FNA as well as the histopathology results from the surgical specimen.	Primary: Diagnostic accuracy, true positives/negatives and false positives/negatives associated with FNA in diagnosing benign versus malignant disease; Secondary: - Results: Study overview: The systematic review yielded 70 criterion-meeting studies, 63 of which contained data that allowed for computation of numerical outcomes (n = 5647 patients; level 2a) and consideration of meta-analysis. Results: Subgroup analyses were performed in studies that were prospective, involved consecutive patients, described the FNA technique utilized, and used ultrasound guidance. The I2 point estimate was >70% for all analyses, except within prospectively obtained and ultrasound-guided results. Among the prospective subgroup, the pooled	70 studies included. See article for list.	

examined adults and/or children presenting with clinically or radiographically identified parotid masses who subsequently underwent parotidectomy; 2. FNA was performed prior to surgery via palpation or ultrasound guidance; 3. the cytopathology results from the FNA as well as the histopathology results from the surgical specimen are both reported; 4. the study denoted true positives/negatives and false positives/negatives associated with FNA in diagnosing benign versus malignant disease; and 5. the study was a randomized or quasi-randomized controlled trial, nonrandomized prospective trial, or retrospective review. Exclusion Criteria: 1. they did not contain sufficient data to determine the number of true positives/negatives and false positives/negatives; 2. they reported on salivary gland pathology as a whole, without distinguishing between parotid and other salivary glands; and		analysis demonstrated a sensitivity of 0.882 (95% confidence interval [95% CI], 0.509–0.982) and a specificity of 0.995 (95% CI, 0.960–0.999). The probabilities of nondiagnostic and indeterminate cytology were 0.053 (95% CI, 0.030–0.075) and 0.147 (95% CI, 0.106–0.188), respectively. Author's Conclusion: FNA of the parotid gland has moderate sensitivity and high specificity in differentiating malignant from benign disease. Given the high positive LR, a positive FNA can predict the presence of malignancy with 98% to 100% accuracy, depending on the prevalence of malignancy. However, patients with a negative FNA may still have a tangible posttest probability of malignancy, particularly if the underlying prevalence of disease is high. Physicians should therefore take the pretest probability of malignancy in their patient populations into account when interpreting parotid FNA results. Significant heterogeneity was found among the included studies, particularly in terms of the classification and reporting of intermediate results. An effort to standardize the classification of parotid FNA findings would improve the consistency with which surgeons interpret and approach intermediate results		

3. they were case reports or abstracts that did not contain sufficient data.				
Methodical Notes				
Funding Sources: Funding source: None. COI: Declared, textbook royalties, universtity grants. See article Study Quality: Quality of studies was assesed, by the authors own criteria. Results are reported for individual studies. "Potential risks of bias were tracked. Specifically, we recorded whether the design of a study was prospective or retrospective, whether consecutive patients were described, whether blinding was employed, whether there was a technical description of the FNA method utilized, and whether FNAs were performed under ultrasound guidance." "The majority of studies had a retrospective or unspecified study design (91%) and involved nonconsecutive series of patients (72%)". Heterogeneity: The I2 statistic was used to evaluate heterogeneity among the included studies. It reflects the degree of variability that is due to more than chance alone. We used the following criteria to interpret the I2 statistic: 0%–40% indicates likely unimportant heterogeneity; 30%–60%, moderate heterogeneity; 50%–90%, significant heterogeneity; 75%–100%, considerable heterogeneity. For our pooled estimates, we present the associated I2 statistic along with its 95% confidence interval (CI). "Considerable heterogeneity was found among studies, with an I2 statistic of 72.4% (95% CI, 65.5%–79.3%) for sensitivity and 78.6% (95% CI, 73.6%–83.6%) for specificity." Publication Bias: The presence of publication bias was assessed by performing a Deeks' funnel plot asymmetry test. $P < .05$ was considered significant for the presence of bias. The overall symmetrical distribution of study estimates suggests that there is no publication bias. A P value of 0.341 supports the visual assessment. Notes: Oxford level of evidence: 3 Systematic review and meta-analysis of diagnostic studies without blinding, predominantly retrospective and nonconsecutive Considerable heterogeneity was found among studies, which limits implications.				

Novoa, E. et al. Role of ultrasound-guided core-needle biopsy in the assessment of head and neck lesions: a meta-analysis and systematic review of the literature. Head Neck. 34. 1497-503. 2012				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 2 Study type: Systematic review and meta-analysis of diagnostic studies (16 studies) To determine the role of CNB in the assessment of head and neck lesions Databases: Cochrane database of randomized controlled trials, PubMed/Medline Search period: Search period not specified. Inclusion Criteria: Only those publications that explicitly reported raw data, comparing the presumptive diagnosis of ultrasoundguided core needle biopsy in the head and neck with definitive histology obtained by excisional biopsy, were finally selected. In some instances, corresponding authors were contacted for patient data when specific information for statistical analysis was required. Exclusion Criteria:	Population: Patients with head and neck lesions. Intervention: Diagnosis of ultrasoundguided core needle biopsy Comparison: Definitive histology obtained by excisional biopsy	Primary: Diagnostic accuracy. Secondary: - Results: Study overview: A systematic review of the literature and meta-analysis of data extracted from 16 included studies were performed. A total of 1291 cervical lesions in 1267 patients were examined by CNB. This resulted in 1232 adequate samples, from which 554 were subsequently confirmed by excisional biopsy. Results: CNB was able to identify true neoplasms and detect malignancy in head and neck lesions with an overall accuracy of 94% and 96%, respectively, even though there was a significant difference between the histologically verified and all adequate samples. CNB provided a correct specific diagnosis in 87% of cases without major complications and achieved a higher accuracy than that of fine-needle aspiration in detecting malignancy Author's Conclusion: This meta-analysis confirms that CNB is an excellent method in the	16 studies, of which 5 studied salivary glands. Buckland 1999, Howlet 2007, Kesse 2002, Taki 2005, Tang 2004	

		assessment of salivary gland lesions and lymphadenopathies inclusive of malignant lymphoma, but it is not ideal for evaluating thyroid lesions.		
Methodical Notes				
Funding Sources: Not declared. COI: Not declared. Study Quality: Unclear, no evaluation of study quality was performed. Heterogeneity: No description or investigation. Publication Bias: No description or investigation. Notes: Oxford level of evidence: 2 systematic review and meta-analysis of diagnostic studies (retrospective and prospective) with consistently applied reference standard. Downgrade to evidence level 3. No assesment of study quality was performed. No investigation of heterogeneity, publication bias. No declaration of conflicts of interest. Only 5 out of 16 studies investigated salivary glands.				
Schmidt, R. L. et al. A systematic review and meta-analysis of the diagnostic accuracy of ultrasound-guided core needle biopsy for salivary gland lesions. Am J Clin Pathol. 136. 516-26. 2011				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	

Evidence level: 3 Study type: Systematic review and meta-analysis of diagnostic studies (64 studies) To summarize the evidence on the diagnostic accuracy of FNAC for parotid gland tumors using current guidelines for systematic review and meta-analysis of diagnostic studies. Databases: MEDLINE, EMBASE, and the bibliographies of retrieved articles Search period: January 1, 1985, and December 31, 2010. Inclusion Criteria: Studies containing data on histologically verified cases involving parotid tumors and provided data that enabled lesions to be classified into broad categories (malignant vs benign and nonneoplastic vs neoplastic). Exclusion Criteria: Studies that included only data on the diagnosis of a particular disease entity. We excluded studies using needle core biopsy and included only studies in which the needle size was 20 gauge or smaller (0.60 mm inner diameter). We excluded case reports and studies with fewer than 10 cases. Eligible studies were included if accuracy data could be extracted in the form required for analysis (true-positives, false-positives, false-negatives, and true-negatives). All studies except 1 reported only cases with histologic verification. In	Population: Patients with parotid gland tumors Intervention: FNAC Comparison: Reference standarad (H&E histologic findings)	Primary: Diagnostic accuracy Secondary: - Results: We identified 64 studies on the diagnosis of malignancy (6,169 cases) and 7 studies on the diagnosis of neoplasia (795 cases). The diagnosis of neoplasia (area under the summary receiver operating characteristic [AUSROC] curve, 0.99; 95% confidence interval [CI], 0.97-1.00) had higher accuracy than the diagnosis of malignancy (AUSROC, 0.96; 95% CI, 0.94-0.97). Several sources of bias were identified that could affect study estimates. Studies on the diagnosis of malignancy showed significant heterogeneity (P < .001). The subgroups of American, French, and Turkish studies showed greater homogeneity, but the accuracy of these subgroups was not significantly different from that of the remaining subgroup. Author's Conclusion: It is not possible to provide a general guideline on the clinical usefulness of FNAC for parotid gland lesions owing to the variability in study results. There is a need to improve the quality of reporting and to improve study designs to remove or assess the impact of bias.	64 studies included, see article.	

that study, 18 there were 67 cases with histologic verification and 4 benign cases with clinical follow-up. We excluded the 4 cases that had only clinical follow-up.				
Methodical Notes				
Funding Sources: The authors of this article and the planning committee members and staff have no relevant financial relationships with commercial interests to disclose. COI: The authors of this article and the planning committee members and staff have no relevant financial relationships with commercial interests to disclose. Study Quality: Quality assessment of articles written in English was conducted using the QUADAS tool by two authors. Summary judgment or individual study results was not provided. Heterogeneity: Method not stated. "There was significant heterogeneity among studies (P < .001)." Publication Bias: Publication bias not investigated. Notes: Oxford level of evidence: 3 Systematic review and meta-analysis of retrospective diagnostic studies with consistently applied reference standard and partially consectutive recruitment and blinding. Significant information in the analyses, but little information regarding the methods. No individual results for the assesment of study quality are provided.				
Schmidt, R. L. et al. A systematic review and meta-analysis of the diagnostic accuracy of fine-needle aspiration cytology for parotid gland lesions. Am J Clin Pathol. 136. 45-59. 2011				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	

Evidence level: 2 Study type: Systematic review and meta-analysis of diagnostic studies (5 studies) To develop a summary ROC (SROC) curve for the diagnostic performance of CNB in the evaluation of salivary gland tumors. Databases: MEDLINE, Embase, and the bibliographies Search period: January 1, 1985, and March 15, 2011, Inclusion Criteria: Studies were included if they contained extractable data on salivary gland lesions, contained histologic verification of all cases, and provided data that enabled lesions to be classified into broad categories (malignant vs benign or neoplastic vs nonneoplastic). Exclusion Criteria: Case reports and studies with fewer than 5 cases. Eligible studies were included if accuracy data could be extracted in the form required for analysis (true-positive, false-positive, false-negative, and truenegative). In cases with overlapping data sets, we included only the most recent comprehensive data.	Population: Patients with salivary gland lesions. Intervention: Ultrasound-Guided Core Needle Biopsy. Comparison: Histologic verification.	Primary: Diagnostic accuracy. Secondary: Histologic verification. Results: We identified 5 studies (277 cases) for inclusion. The area under the SROC for CNB was 1.00 (95% confidence interval [CI], 0.99-1.00). Based on histologically verified cases, the sensitivity of CNB is 0.92 (95% CI, 0.77-0.98) and the specificity is 1.00 (95% CI, 0.76-1.00). Author's Conclusion: "We conclude that CNB has high accuracy and a low (1.2%) inadequacy rate. CNB is more accurate than fine-needle aspiration, at least in some settings, but the best selection of which test to use for an individual patient and setting remains to be defined."	5 studies included: Breeze 2009, Naqvi 2008, Taki 2005, Wan 2004, Yamashita 2002.	
Methodical Notes				

Funding Sources: "The authors of this article and the planning committee members and staff have no relevant financial relationships with commercial interests to disclose." COI: See funding section. Study Quality: Quality assessment of articles was conducted by using the QUADAS tool. Assessment was completed independently by 2 authors using a scoring form, and discrepancies were resolved by consensus. Results of the quality assesment are available, but no individual results are displayed or overall judgment was provided. Heterogeneity: Heterogeneity was tested using the I2 statistic15,16 and the Cochrane Q statistic using the log-rank test. "The degree of heterogeneity observed in this collection of studies was statistically insignificant (log-rank Cochrane Q = 0.10; df = 2; P = .48). Thus, there is much less variation in diagnostic performance of CNB compared with FNAC" Publication Bias: Not feasible, less than 10 studies included. Notes: Oxford level of evidence: 2 Systematic review and meta-analysis of diagnostic studies with consistently applied reference standard and blinding in some studies. No individual results for the assesment of study quality.	

Witt, B. L. et al. Ultrasound-guided core needle biopsy of salivary gland lesions: a systematic review and meta-analysis. Laryngoscope. 124. 695-700. 2014				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 3 Study type: Systematic review and meta-analysis of diagnostic studies (5 studies) To obtain summary estimates of the sensitivity and specificity of core needle	Population: Patients with salivary gland lesions. Intervention: Core needle biopsy	Primary: Diagnostic accuaracy, sensitivity, specificity Secondary: - Results: The summary estimates of sensitivity and specificity of core needle biopsy for diagnosis of	5 studies included in the analysis: Breeze 2009, Huang 2012, Naqvi 2008,	

biopsy for assessment of salivary gland lesions and to investigate sources of variation in accuracy between study locations. Databases: The Pubmed, Embase, CAB Abstracts, CINAHL, Web of Science, BIOSIS, Trip Database, PakMediNet, LILACS, IndMED, National Guidelines Clearinghouse, ARIF, and Medion databases were searched on January 16, 2012. Search period: Inception - January 16, 2012. Inclusion Criteria: Diagnostic accuracy studies compared diagnoses of salivary gland lesions obtained by CNB to a reference standard (histopathology or clinical follow-up). There were no restrictions on study design, language, or time period. Exclusion Criteria: -	Comparison: Reference standard (histopathology or clinical follow-up).	malignancy were 96% (95% confidence interval [CI] 87–99) and 100% (95% CI 84–100), respectively. There was no significant heterogeneity in accuracy between studies. The quality of included studies was high, with low risk of verification bias. The risk of hematoma was 1.6% per procedure. Author's Conclusion: Core needle biopsy has high sensitivity and specificity, and has low risk of complications. There is no significant variation in accuracy between study locations.	Pfeiffer & Ridder 2012, Taki 2005.	
Methodical Notes				
Funding Sources: The authors have no funding, financial relationships, or conflicts of interest to disclose. COI: The authors have no funding, financial relationships, or conflicts of interest to disclose. Study Quality: Risk of bias and comparability was independently assessed by two reviewers using the QUADAS-2 instrument.				

The quality of the included studies was generally high. All of the included studies had complete follow-up (histology or clinical observation). Heterogeneity: Method not specified. There was no significant heterogeneity in accuracy between studies because of the strict methods we incorporated for study inclusion in this review. Publication Bias: Not investigated, but not feasible with less than 10 studies. Notes: Oxford level of evidence: 3 Systematic review of and meta-analysis of diagnostic studies with consistently applied reference standard, but no information regarding blinding, consecutive recruitment or prospective/retrospective evaluation Some, but not complete overlap in primary studies with Novoa 2012.	

1.2 Sammlung 01b. Welche diagnostischen Verfahren sind bei der Identifikation von Raumforderungen der Speicheldrüsen effektiv? Excision, biopsy vs Bildgebende Verfahren

OXFORD (2011) Appraisal Sheet: Systematic Reviews

Li, C. et al. Compression Real-time Elastography for Evaluation of Salivary Gland Lesions: A Meta-analysis. J Ultrasound Med. 35. 999-1007. 2016				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 2 Study type: Systematic review and meta-analysis of diagnostic studies (9 studies) To evaluate the performance of compression real-time elastography for differentiation between benign and malignant salivary gland lesions. Databases: PubMed, Embase, Ovid, Cochrane Library, China National Knowledge Infrastructure, Chongqing VIP, Chinese Biomedical Literature and Google Scholar databases Search period: Inception - June 31, 2015. Inclusion Criteria: First, the articles	Population: Patients with salivary gland lesions. Intervention: Real-time elastography Comparison: Histopathologic analysis as the reference standard	Primary: Diagnostic accuracy for differentiation of benign from malign lesions. Secondary: - Results: 9 articles with 581 lesions were included. The pooled sensitivity and specificity of real-time elastography for differentiation between benign and malignant lesions were 76% (95% confidence interval [CI], 65%–85%; 95% prediction interval [PI], 29%–95%) and 73% (95% CI, 62%–81%; 95% PI, 24%–96%), respectively. The LR+ and LR– were 2.81 (95% CI, 1.79–4.39; 95% PI, 0.65–12.16) and 0.33 (95% CI, 0.20– 0.55; 95% PI, 0.07–1.69). The area under the ROC curve	9 Studies included: Bhatia et al 2010, Dumitriu et al 2010, Dumitriu et al 2011, Li et al 2012, Ye et al 2012, Yerli et al 2012, Celebi et al 2013, Du et al 2015, Yuan et al 2015.	

evaluated the effects of real-time elastography for diagnosis of salivary gland lesions with quantitative determination. Second, the diagnosis was confirmed by using histopathologic analysis as the reference standard. Third, the studies provided available data for constructing 2 × 2 contingency tables. Fourth, the studies enrolled at least 30 salivary gland nodules. Exclusion Criteria: Studies such as reviews, case reports, editorials, letters, commentaries, and conference proceedings were excluded		was 0.81 (95% CI, 0.77– 0.84). No publication bias was detected, according to the Deek funnel plot (P = .51). The Fagan plot showed that when pretest probabilities were 25%, 50%, and 75%, positive posttest probabilities were 48%, 74%, and 89%, and negative probabilities were 10%, 25%, and 50%. Author's Conclusion: Real-time elastography is a novel supplementary adjunct to conventional sonography for evaluation of salivary gland lesions. However, its overall accuracy is less promising, and biopsy may still be necessary in routine clinical practice.		
Methodical Notes				
Funding Sources: not declared. COI: not declared. Study Quality: The QUADAS quality assessment tool was used to evaluate each study. The overall quality of the studies was good, but none of the included studies received a positive response to questions 4 and 11. Heterogeneity: Heterogeneity was tested by the I2 inconsistency index and $\chi 2$ test. I2 > 50% suggests that more heterogeneity exists beyond that from chance.10 As for the $\chi 2$ test, P < .05 confirmed the existence of heterogeneity between studies.11 Therefore, if I2 > 50% or P < .05, a random-effects model was applied in the analysis; otherwise, a fixed-effect model was used. The included studies were statistically heterogeneous in the estimates of sensitivity (I2 = 51.85%; P= .03) and specificity (I2 = 81.21%; P< .01). Publication Bias: A Deek funnel plot was used to assess publication bias in the included studies.				

According to the Deek funnel plot asymmetry test, no publication bias was detected among the studies (P = 0.51) Notes: Oxford level of evidence: 1 Systematic review and meta-analysis of prospective diagnostic studies with consistently applied reference standard, but not blinding. No declaration of conflicts of interest.				
Liang, Y. Y. et al. accuracy of magnetic resonance imaging techniques for parotid tumors, a systematic review and meta-analysis. Clinical Imaging. 52. 36-43. 2018				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 3 Study type: Systematic review and meta-analysis of diagnostic studies (14 studies) To assess the added benefit of combining different MRI techniques for preoperative diagnosis of parotid tumors when compared to conventional MRI and advanced MRI techniques alone with meta-analysis. Databases: PubMed. Search period: Inception - 07/2017. Inclusion Criteria: All available prospective and retrospective studies that had patients with parotid tumors in all age groups performing conventional or advanced MRI or the combination of conventional and advanced MRI were included. Studies were included if 2x2 tables could be extracted.	Population: Patients with parotid tumors. Intervention: Advanced MRI techniques alone or in combination. Comparison: Conventional MRI	Primary: Diagnostic accuracy, positives (TP), false positives(FP), true negatives(TN), false negatives(FN). Secondary: - Results: Pooled sensitivity and specificity of conventional MRI, diffusion weighted imaging (DWI), dynamic contrast enhanced (DCE) and the above combination were 76% (95%CI)/ 91% (95%CI)/ 80% (95%CI)/ 86% (95%CI) and 83% (95%CI)/ 56% (95%CI)/ 90% (95%CI)/ 90% (95%CI). Author's Conclusion: Conventional MRI combined with DWI and DCE showed higher diagnostic accuracy than conventional or advanced MRI alone, supporting their use in parotid tumors diagnosis.	14 studies included: Abdel 2017, Inohara 2008, Lechner 2011, Mikaszewski 2017, Stefanovic 2016, Takashima 2001, Tao 2017, Yabuuchi 2008, Yerli 2010.	

The definitive diagnosis was established by fine-needle aspiration biopsy, aspiration biopsy and radiologic follow-up, surgical biopsy, surgical resection. Exclusion Criteria: Editorials, letters to the editor, review articles, case reports, animal experimental studies and studies with no detailed information about the diagnostic and quantitative accuracy of MR imaging were excluded.				
Methodical Notes				
Funding Sources: not stated. COI: not stated. Study Quality: The methodologic quality of each study was evaluated by two independent reviewers who used the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool. Each study was judged as “Yes (low risk of bias),” “No (high risk of bias),” or “Unclear.” Study quality was considered to be high or unclear risk of bias in all cases. Heterogeneity: The inconsistency index (I2) were used to assess the heterogeneity of the included studies. Forest plots were drawn to show comparisons of the odds ratio and 95% CI between the study groups. A significance level of P <0.05 in combination with an I2 > 50% indicates significant heterogeneity. If marked heterogeneity was observed, the diagnostic performance was summarized using a random-effects model. Publication Bias: For the overall studies, the statistically non significant P value (0.738) for the slope coefficient indicated the symmetry in the data and a low likelihood of publication bias. Similarly, except for the ADC group with only two studies, for the remaining three subgroup datasets, with all the P values greater than 0.05, it indicated the symmetry in all the data and a low likelihood of publication bias. Notes: Oxford level of evidence: 2 Systematic review and meta-analysis of diagnostic studies with consistently applied reference standard, but not blinding				

(retrospective and prospective). Downgrade to evidence level 3. Using only one database is not considered a comprehensive search. High heterogeneity was observed for the specificity outomce. Study quality was considered to be high or unclear in at least one domain per study. No declaration of conflicts of interest.	

Schmidt, R. L. et al. A systematic review and meta-analysis of the diagnostic accuracy of ultrasound-guided core needle biopsy for salivary gland lesions. Am J Clin Pathol. 136. 516-26. 2011

Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 3 Study type: Systematic review and meta-analysis of diagnostic studies (64 studies) To summarize the evidence on the diagnostic accuracy of FNAC for parotid gland tumors using current guidelines for systematic review and meta-analysis of diagnostic studies. Databases: MEDLINE, EMBASE, and the bibliographies of retrieved articles Search period: January 1, 1985, and December 31, 2010. Inclusion Criteria: Studies containing data on histologically verified cases involving parotid tumors and provided data that enabled lesions to be classified into broad categories (malignant vs benign and nonneoplastic vs neoplastic). Exclusion Criteria: Studies that included only data	Population: Patients with parotid gland tumors Intervention: FNAC Comparison: Reference standarad (H&E histologic findings)	Primary: Diagnostic accuracy Secondary: - Results: We identified 64 studies on the diagnosis of malignancy (6,169 cases) and 7 studies on the diagnosis of neoplasia (795 cases). The diagnosis of neoplasia (area under the summary receiver operating characteristic [AUSROC] curve, 0.99; 95% confidence interval [CI], 0.97-1.00) had higher accuracy than the diagnosis of malignancy (AUSROC, 0.96; 95% CI, 0.94-0.97). Several sources of bias were identified that could affect study estimates. Studies on the diagnosis of malignancy showed significant heterogeneity (P < .001). The subgroups of American, French, and Turkish studies showed greater homogeneity, but the accuracy of these subgroups was not significantly different from that of the remaining subgroup.	64 studies included, see article.	

on the diagnosis of a particular disease entity. We excluded studies using needle core biopsy and included only studies in which the needle size was 20 gauge or smaller (0.60 mm inner diameter). We excluded case reports and studies with fewer than 10 cases. Eligible studies were included if accuracy data could be extracted in the form required for analysis (true-positives, false-positives, false-negatives, and true-negatives). All studies except 1 reported only cases with histologic verification. In that study, 18 there were 67 cases with histologic verification and 4 benign cases with clinical follow-up. We excluded the 4 cases that had only clinical follow-up.		Author's Conclusion: It is not possible to provide a general guideline on the clinical usefulness of FNAC for parotid gland lesions owing to the variability in study results. There is a need to improve the quality of reporting and to improve study designs to remove or assess the impact of bias.		
Methodical Notes				
Funding Sources: The authors of this article and the planning committee members and staff have no relevant financial relationships with commercial interests to disclose. COI: The authors of this article and the planning committee members and staff have no relevant financial relationships with commercial interests to disclose. Study Quality: Quality assessment of articles written in English was conducted using the QUADAS tool by two authors. Summary judgment or individual study results was not provided. Heterogeneity: Method not stated. "There was significant heterogeneity among studies (P < .001)." Publication Bias: Publication bias not investigated. Notes:				

Oxford level of evidence: 3 Systematic review and meta-analysis of retrospective diagnostic studies with consistently applied reference standard and partially consectutive recruitment and blinding. Significant information in the analyses, but little information regarding the methods. No individual results for the assesment of study quality are provided.				
Witt, B. L. et al. Ultrasound-guided core needle biopsy of salivary gland lesions: a systematic review and meta-analysis. Laryngoscope. 124. 695-700. 2014				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 3 Study type: Systematic review and meta-analysis of diagnostic studies (5 studies) To obtain summary estimates of the sensitivity and specificity of core needle biopsy for assessment of salivary gland lesions and to investigate sources of variation in accuracy between study locations. Databases: The Pubmed, Embase, CAB Abstracts, CINAHL, Web of Science, BIOSIS, Trip Database, PakMediNet, LILACS, IndMED, National Guidelines Clearinghouse, ARIF, and Medion databases were searched on January 16, 2012. Search period: Inception - January 16, 2012. Inclusion Criteria: Diagnostic accuracy studies compared diagnoses of salivary	Population: Patients with salivary gland lesions. Intervention: Core needle biopsy Comparison: Reference standard (histopathology or clinical follow-up).	Primary: Diagnostic accuaracy, sensitivity, specificity Secondary: - Results: The summary estimates of sensitivity and specificity of core needle biopsy for diagnosis of malignancy were 96% (95% confidence interval [CI] 87–99) and 100% (95% CI 84–100), respectively. There was no significant heterogeneity in accuracy between studies. The quality of included studies was high, with low risk of verification bias. The risk of hematoma was 1.6% per procedure. Author's Conclusion: Core needle biopsy has high sensitivity and specificity, and has low risk of complications. There is no significant variation in accuracy between study locations.	5 studies included in the analysis: Breeze 2009, Huang 2012, Naqvi 2008, Pfeiffer & Ridder 2012, Taki 2005.	

gland lesions obtained by CNB to a reference standard (histopathology or clinical follow-up). There were no restrictions on study design, language, or time period. Exclusion Criteria: -				
Methodical Notes				
Funding Sources: The authors have no funding, financial relationships, or conflicts of interest to disclose. COI: The authors have no funding, financial relationships, or conflicts of interest to disclose. Study Quality: Risk of bias and comparability was independently assessed by two reviewers using the QUADAS-2 instrument. The quality of the included studies was generally high. All of the included studies had complete follow-up (histology or clinical observation). Heterogeneity: Method not specified. There was no significant heterogeneity in accuracy between studies because of the strict methods we incorporated for study inclusion in this review. Publication Bias: Not investigated, but not feasible with less than 10 studies. Notes: Oxford level of evidence: 3 Systematic review of and meta-analysis of diagnostic studies with consistently applied reference standard, but no information regarding blinding, consecutive recruitment or prospective/retrospective evaluation Some, but not complete overlap in primary studies with Novoa 2012.				
Zhang, Y. F. et al. Sonoelastography for differential diagnosis between malignant and benign parotid lesions: a meta-analysis. European Radiology. 29. 725-735. 2019				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	

Evidence level: 3 Study type: Systematic review and meta-analysis (10 studies) To assess the performance of sonoelastography for differential diagnosis between malignant and benign parotid lesions using a meta-analysis. Databases: PubMed, Embase and Medline (Embase. com), Web of Science, Cochrane Library and Ovid. Search period: Inception - 30 October 2017. Inclusion Criteria: (1) The study was approved by an ethics committee or institutional review board. (2) The diagnostic performance of sonoelastography for the differential diagnosis between malignant and benign parotid lesions was evaluated in the study. (3) Postoperative pathology and/or fine-needle aspiration cytology (and/or histology) results were used as the reference standard in the study. (4) Complete reported data were available to calculate the true positive (TP), false positive (FP), false negative (FN) and true negative (TN) cases	Population: Patients with parotid lesions. Intervention: Sonoelastography Comparison: reference standard (histopathology and/or cytology)	Primary: Diagnostic accuracy for differential diagnosis Secondary: - Results: "10 eligible studies that included a total sample of 711 patients with 725 parotid lesions were included. Sonoelastography showed a pooled sensitivity of 0.67 (95% CI 0.59–0.74), specificity of 0.64 (95% CI 0.60–0.68), DOR of 8.00 (95% CI 2.96–21.63) and an AUC of 0.77. The results of the meta-regression analysis revealed that no heterogeneity was due to the imaging mechanism (p = 0.119), shear wave elastography technique (p = 0.473) or QUADAS score (p = 0.462). However, the assessment method was a significant factor that affected the study heterogeneity (p = 0.035). According to the subgroup analysis, quantitative and semiquantitative methods performed better than qualitative ones." Author's Conclusion: "Overall, sonoelastography has a limited value for differential diagnosis between malignant and benign parotid lesions. Quantitative and semiquantitative methods perform better than qualitative ones."	10 studies included: Klintworth 2012, Yerli 2012, Badea 2013, Celebi & Mahmutoglu 2013, Wierzbicka 2013, Yu 2016, Altinbas 2017, Cantisani 2017, Herman 2017, Mansour 2017.	

Exclusion Criteria: (1) Reviews, case reports, letters, conference reports, editorial comments and articles that were not published in English were excluded. (2) In studies with insufficient data, the corresponding authors were contacted and requested to provide the missing data via e-mail. The studies were excluded if the author did not reply within 15 days. (3) When two or more studies were performed by the same department, the study that was older or that had the smaller number of patient samples was excluded.				
Methodical Notes				
Funding Sources: The authors state that this work has not received any funding. COI: The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article. Study Quality: The methodological qualities of primary studies were assessed with the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) criteria. Most of the studies were high quality according to the QUADAS questionnaire. A meta-regression revealed that the QUADAS score was not a significant factor affecting study heterogeneity. Heterogeneity: The heterogeneity was evaluated by the Cochran Q statistic and the I2 test. A random effects model was usedwhen the p value of heterogeneity was less than 0.05 or the I2 was at least 50%, otherwise a fixed effects model was used. Potential sources of heterogeneity were explored with a meta-regression analysis. Considerable heterogeneity was present for sensitivity, specificity and AUC. The assessment method was revealed to be a major source of heterogeneity in meta-regression.				

Publication Bias: Deeks' funnel plot was generated in STATA to analyse the potential publication bias, with a $p < 0.05$ indicating potential publication bias. Deeks' funnel plots showed no significant publication bias. Notes: Oxford level of evidence: 3 Systematic review and meta-analysis of diagnostic with consistently applied reference standard with blinding in some but not all studies, but no information regarding consecutive recruitment or prospective retrospective evaluation. Considerable heterogeneity was for all outcomes, which limits implications.	

1.3 Sammlung 01c. Welche diagnostischen Verfahren sind bei der Identifikation von Raumforderungen der Speicheldrüsen effektiv? Ultraschall vs. andere bildgebende Verfahren

OXFORD (2011) Appraisal Sheet: Systematic Reviews

Bertagna, F. et al. Diagnostic role of (18)F-FDG-PET or PET/CT in salivary gland tumors: A systematic review. Rev Esp Med Nucl Imagen Mol. 34. 295-302. 2015				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 2 Study type: Systematic review of diagnostic studies (22 articles) To evaluate the diagnostic performance of PET in this particular setting,analyzing the available literature. Databases: PubMed/MEDLINE, Embase and Scopus including references of the retrieved articles Search period: Inception - 30th November 2014. Inclusion Criteria: Studies or subsets in studies investigating the role of 18F-FDG-PET or PET/CT in patients with SGTs. Exclusion Criteria: (a) articles not in the field of	Population: Patients with salivary gland tumors. Intervention: 18F-FDG-PET or PET/CT Comparison: reference standard (not specifed).	Primary: Diagnostic accuracy. Secondary: - Results: 22 articles were included. The studies selected suggest that: (1) PET is not useful in discriminating benign frommalignant SGTs because of the overlap of uptake in both conditions; (2) PET not only is complementary toconventional imaging techniques for the staging and restaging but in some cases could also be superiorto them; (3) PET may often have a highly positive impact on clinical decision making. Author's Conclusion: Despite manylimitations affecting the analysis, PET seems to be useful in	22 studies are included, list see article.	

interest of this review; (b) review articles, editorials or letters, confer-ence proceedings; (c) case reports or small case series (<10patients). Only those studies including whole-body18F-FDG-PETor PET/CT scans performed in patients with SGTs were included		SGTs. However, more extensive studies and cost-effectiveness analyses are desirable to determine its correct position in the diagnostic flow chart.		
Methodical Notes				
Funding Sources: Not disclosed. COI: The authors declare that they have no conflict of interest. Study Quality: Study quality was not assesed. Heterogeneity: No meta analysis was performed, due to high heterogeneity. Publication Bias: No investigated. Notes: Oxford level of evidence: 1 Systematic review Dwongrade to evidence level 2. Reference standard not specified. No meta-analysis was performed due to heterogeneity. The authors claim that this stems from differences in the reference standard. Study quality was not assesed.				

Haldrup, M. et al. Utility of ultrasound of the lymph nodes in patients with high-risk cutaneous squamous cell carcinoma. European Journal of Plastic Surgery. 41. 619-624. 2018

Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 3 Study type: Systematic review of diganostic	Population: Patients with squamous cell carcinoma of the head	Primary: Sensitivity, specificity and negative predictive value (NPV) were calculated for each study and a cumulative calculation was made	8 studies included: total n = 664 Souren et al. 2016,	

studies with consistently applied reference standard but not blinding. (8 studies) To evaluate ultrasound in the diagnostics of lymph node metastases in cutaneous squamous cell carcinoma and in the light of different Bhigh-risk^ factors in cSCC to evaluate who would benefit from US. Databases: PubMed, Embase and Cochrane Search period: 2000 until September 2017. Inclusion Criteria: Studies containing information about US used for examination of lymph nodes of the neck in HNSCC were included. Further, only articles based on histologically evaluated pathology of the lymph nodes were included. Histologically examination was considered gold standard in all included articles. Lastly, articles included had to contain information on sensitivity and specificity for US from the lymph nodes. Patients in the different included studies were selected for undergoing US (and different other modalities varying in the studies) if they had a previously untreated, histology proven SCC of the head and neck Exclusion Criteria: Casuistic studies and studies that did not differentiate between	neck (HNSCC) Intervention: US Comparison: CT, PET CT	Secondary: - Results: Sensitivity for US for the total cohort was 85.9, specificity was 96.3%, negative predictive value (NPV) was 93.1% and accuracy was 92.2%. We found significantly no difference when US was compared to CT and PET CT. CT had a sensitivity, specificity, NPV and accuracy at 82.8, 97.7, 90.9 and 92.32%respectively. Sensitivity, specificity, NPVand accuracy for PET CT were 87.4, 98.1, 95.2 and 95.2% respectively. In contrast,we found clinical examination to have the significantly lowest sensitivity, specificity, NPV and accuracy at 69.6, 80, 61.1 and 73.4%, respectively. Author's Conclusion: Ultrasound is found to have equal sensitivity, specificity and NPV as CT and PET CT. Further, US is proven significant better than clinical examination. Patients with one or two high-risk factors for metastases could very well benefit from US of neck. However, more studies on US are necessary and further, specific studies on cSCC should be performed in order to see if US of the neck in HNSCC patients is transferable to cSCC. Level of evidence: Not ratable.	Safaan et al. 2013, Stoeckli et al. 2011, Yoon et al. 2009, Akoglu et al. 2005, Thomasen et al. 2005, Haberal et al. 2004, Jank et al. 2002, Stukesen et al. 2002	

cSCC of the head and neck and the rest of the body were excluded.				
Methodical Notes				
Funding Sources: not declared. COI: Declared, none present. Study Quality: No evaluation of study quality. Heterogeneity: No meta-analysis was performed. Publication Bias: Less than 10 studies were included, No meta-analysis was performed. Notes: Oxford level of evidence: 2 Systematic review of diagnostic studies without consistently with consistently applied reference standard, but not blinding or information regarding consecutive recruitment. Downgraded to evidence level 3 due to poor quality. No search for grey literature. Only English literature was searched. Unclear if selection or data extraction were carried out by more than one investigator. No evaluation of study quality.				

Kong, X. et al. The diagnostic role of ultrasonography, computed tomography, magnetic resonance imaging, positron emission tomography/computed tomography, and real-time elastography in the differentiation of benign and malignant salivary gland tumors: a meta-analysis. Oral Surg Oral Med Oral Pathol Oral Radiol. 128. 431-443.e1. 2019				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	

Evidence level: 2 Study type: Systematic review and meta-analysis of diagnostic studies (38 studies) To assess the diagnostic properties of ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography/computed tomography (PET/CT), and real-time elastography (RTE) in distinguishing between benign and malignant salivary gland tumors Databases: PubMed, ScienceDirect, and Web of Science databases Search period: Inception - January 2019 Inclusion Criteria: (1) use of ultrasonography, CT, MRI, PET/CT, or RTE to differentiate benign from malignant salivary gland tumors; (2) comparison of the diagnostic results of the imaging modalities with a reference standard; and (3) provision of sufficient data for constructing 2£ 2 contingency tables. Exclusion Criteria: Citations that did not meet the aforementioned criteria, review studies, case reports, comments, unpublished materials, and studies published in abstract form were excluded.	Population: Patients with salivary gland tumors Intervention: ultrasonography, CT, MRI, PET/CT, or RTE Comparison: reference standard (not specified)	Primary: Accuracy of differention between benign and malignant tumors Secondary: - Results: In total, 38 studies were included. Pooled sensitivities for ultrasonography, CT, MRI, PET/CT, and RTE were 0.66, 0.70, 0.80, 0.81, and 0.80, respectively. Pooled specificities were 0.92, 0.73, 0.90, 0.89, and 0.70, respectively. The DORs were 23, 6, 38, 20, and 10, respectively. The areas under the curve (AUC) of SROC for US, CT, MRI, PET/CT, and RTE were 0.91, 0.77, 0.92, 0.88, and 0.82, respectively. Author's Conclusion: Based on the results of the meta-analysis, MRI may be the first choice for the differential diagnosis of benign and malignant salivary gland tumors for its relatively high diagnostic value. PET/CT tends to have greater accuracy than CT. Ultrasonography and RTE may help achieve better diagnostic outcomes if they are used in conjunction.	38 studies included, see article for list.	
Methodical Notes				

Funding Sources: This research is supported by Beijing Municipal Administration of Hospitals Incubating Program (code: PX2019057). COI: No declaration of conflcits of interest. Study Quality: The quality assessment of diagnostic accuracy study form (QUADAS-2) was used as the guideline. By judging 4 domains (patient selection, index test, reference standard, and flow and timing), each study was ranked as having high, unclear, or low risk of bias. According to the results of the QUADAS-2 items, high risk of bias was mostly observed in the “index test” category, other domains were low or unclear risk. Heterogeneity: Heterogeneity of each study group was tested using the x2 test and the inconsistency index (I2). An I2 greater than 50% and P value of the x2 test less than .05 confirmed the existence of significant heterogeneity, and a random effect model was chosen to pool the data. Otherwise, a fixed-effect model was used. High heterogeneity among the included studies was a major problem. Although meta-regression and subgroup analyses ruled out the influence of some factors on the study results, there were still other variances, such as patient demographic characteristics, specific devices used in evaluation, and cutoff values, which need to be considered. Publication Bias: Publication bias was analyzed by using the Deeks funnel plot and an asymmetry test. According to the Deeks funnel plot asymmetry test, no publication bias was detected among the studies in the ultrasonography (P =.87), CT (P = .84), MRI (P = .22), PET/CT (P = .69), or RTE (P = .98) groups. Notes: Oxford level of evidence: 2 Systematic review and meta-analysis of diagnostic studies with consistently applied reference standard; with blinding in some studies and both retrospective and retrospective study desgin (but with subgroup analysis for prospective/blinding) Reference not defined in inclusion criteria. No declaration of conflcits of interest. High heterogeneity limits implication.	

OXFORD (2011) Appraisal Sheet: Diagnostic Studies

Hung, D. S. W. et al. Ultrasound-guided versus free-hand fine-needle aspiration cytology of the parotid gland: A single-centre, retrospective review. Surgical Practice. 22. 111-115. 2018				
Evidence level/Study Types	Population	Outcomes/Results		
Evidence level: 3 Study type: Retrospective study design. "To evaluate the accuracy and yield of free-hand FNAC versus ultrasound-guided FNAC and its subsequent correlation to the final pathology in order to evaluate its use as a preoperative investigational tool."	Number of patients / samples: 155 Patients who underwent in the Queen Elizabeth Hospital, Hong Kong, by the general surgical team during between 1 January 2008 and 31 March 2016. Reference standard: free-hand FNAC and histopathological diagnosis Validation: Ultrasound-guided FNAC and histopathological diagnosis Blinding: No blinding was performed. Inclusion of clinical information: not reported. Dealing with ambiguous clinical findings: not reported.	Results: Ultrasound-guided FNAC had 100 per cent specificity, whereas free-hand FNAC had 98.3 per cent specificity for detecting malignancy. Sensitivity was 92.9 per cent in the ultrasound-guided FNAC group versus 90 per cent in the free-hand FNAC group. Ultrasound-guided FNAC offered a preoperative diagnosis as to whether a mass was benign or malignant in 21 out of 75 patients (28 per cent), while free-hand FNAC was able to do so in 15 out of 80 patients (18.8 per cent). However, this was not statistically significant (P = 0.188). Author conclusions: Overall, both ultrasound-guided and free-hand FNAC have high sensitivity and specificity for diagnosing malignancy preoperatively. Free-hand FNAC does not have a lower yield and was not shown to be statistically inferior to ultrasound-guided FNAC. Free-hand FNAC is a good alternative in certain cases where the parotid lesion can be easily accessible.		
Methodical Notes				
Funding Sources: not disclosed.				

COI: "The authors report no conflicts of interest" Notes: Oxford level of evidence: Retrospective diagnostic study with consistently applied reference standard without blinding.				
Wang, P. et al. Lymphoepithelial carcinoma of salivary glands: CT and MR imaging findings. Dentomaxillofac Radiol. 46. 20170053. 2017				
Evidence level/Study Types	Population	Outcomes/Results		
Evidence level: 3 Study type: Retrospective diagnostic study without blinding, but with consistently applied reference standard	Number of patients / samples: 103 salivary gland LEC (lymphoepithelial carcinoma) patients. Reference standard: surgical treatment and histopathological examination Validation: CT and MRI Blinding: No blinding was performed. Inclusion of clinical information: not reported. Dealing with ambiguous clinical findings: not reported.	Results: Based on the pathological outcomes, all the salivary gland LECs were classified into two types from CT and MRI scans: solitary LEC (56 cases, 54.4%) and multiple LEC (47 cases, 45.6%). The latter included solitary salivary gland LEC with extraglandular lymphnode metastases (12 cases), parotid gland LEC with ipsilateral intraglandular lymph-node metastases (11 cases), parotid gland LEC with ipsilateral intra- and extraglandular lymphnode metastases (23 cases) and bilateral parotid gland LEC (1 case). The salivary gland LEC was depicted on CT and MRI scans as a lobular mass in 64 of 104 (61.5%), homogeneous mass in 65 of 104 (62.5%) or enhanced neoplasm in 94 of 104 (90.4%). Author conclusions: Salivary gland LEC has a predilection for females in the fourth to fifth decade of life and the parotid gland. CT and MRI findings between solitary and multiple salivary LECs vary. A majority of multiple parotid gland LECs are characterized by metastasis of ipsilateral intraglandular lymph nodes, which may accompany with or without extraglandular lymph-node metastases		
Methodical Notes				
Funding Sources: not declared.				

COI: not declared. Notes: Oxford level of evidence: 3 Retrospective diagnostic study without blinding, but with consistently applied reference standard. No declaration of funding or potential conflicts of interest. No blinding was performed.		

1.4 Sammlung 02 Welche pathohistologischen Verfahren sind geeignet Malignitätskriterien effektiv zu detektieren?

OXFORD (2011) Appraisal Sheet: Systematic Reviews

Colella, G. et al. Fine-needle aspiration cytology of salivary gland lesions: a systematic review. J Oral Maxillofac Surg. 68. 2146-53. 2010				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 3 Study type: Systematic review of diagnostic studies (16 studies) The aim of this study was to provide a systematic review of fine-needle aspiration (FNA) cytology on salivary gland lesions. Databases: National Library of Medicine (Medline), EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL). Search period: January 1990 and January 2009	Population: Patientss with salivary gland lesions. Intervention: FNA Comparison: Histology	Primary: Diagnostic accuracy Secondary: - Results: Of the patients, 484 received a histological diagnosis of malignant tumor; cytological diagnosis was concordant in 387 (79.95%), discordant in 97 (20.04%). A total of 1,275 patients received a histological diagnosis of benign tumor; cytological diagnosis was concordant in 1,219 (95.608%) and discordant in 56 (4.39%). In all, 154 patients received a histological diagnosis of non-neoplastic lesion; cytological diagnosis was	16 studies included 2018 patients: Jayaram 1994, Filopoulos 1998, Al-Khafaji 1998, Feld 1999, Costas 2000, Nasuti 2000, Zbären 2001, Raymond 2002, Sahai 2002, Verma & Kapila 2002, Contucci 2003, Haberal 2003, Postema 2003, Zbären 2004, Aversa 2006, Tan 2006.	

Inclusion Criteria: 1) the study was a randomized or nonrandomized clinical trial, cohort, or case-control study, 2) it enrolled human subjects, 3) there was a correlation reported between FNA diagnosis and histological results, 4) it reported every single histological diagnosis for false positives and false negatives, 5) it was in English, and 6) it was published between 1990 and 2006. Exclusion Criteria: -		concordant in 145 (94.156%) and discordant in 9 (5.84%). Author's Conclusion: FNA is a safe diagnostic tool that has a reliable sensitivity and specificity for the assessment of salivary gland pathology. FNA cytology may be useful in routine preoperative diagnostic testing		
Methodical Notes				
Funding Sources: Supported in part by grants from Ministry of University and Research, Program of Scientific Research of Relevant National Interest. COI: Not declared. Study Quality: Not investigated. Heterogeneity: Not applicable Publication Bias: Not applicable Notes: Oxford level of evidence: 2 Systematic review of diagnostic studies without blinding, and no description of type of study included (likely retrospective) but with consitent application of reference standard. Downgraded to evidence level 3: No declaration of potential conflicts of interest. Only English studies were searched. No evaluation of study quality.				

Farahani, S. J. et al. Retrospective assessment of the effectiveness of the Milan system for reporting salivary gland cytology: A systematic review and meta-analysis of published literature. Diagn Cytopathol. 47. 67-87. 2019				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 3 Study type: Systematic review and meta-analysis of diagnostic studies (92 studies) To determine the accuracy of FNA in detecting salivary gland neoplasms and malignancies, employing the "Milan System for Reporting Salivary Gland Cytopathology" (MSRSGC). Databases: PubMed/ MEDLINE, Embase, and Scopus database and reference lists of identified articles. Search period: Inception - but no endpoint of search Inclusion Criteria: Studies written in English language and which evaluated the diagnostic performance of FNA in detecting salivary gland tumors and differentiating malignant from benign neoplasms and/or neoplasms from nonneoplastic lesions. Exclusion Criteria: Review, case reports, commentary, and editorials or abstracts were excluded. Moreover, studies were also excluded if	Population: Patients with salivary gland tumors Intervention: FNA Comparison: Not specified in inclusion criteria: (histopathologic follow-up);	Primary: Diagnostic accuracy using "Milan System for Reporting Salivary Gland Cytopathology". Risk of malignancy (ROM) was calculated. Secondary: - Results: Study overview: 92 studies with a total of 16 456 FNA with surgical follow-up were included. The pooled data comprised of 31 852 cases of salivary gland tumors, which included 908 cases with only clinical follow-up, 3963 cases of surgically resected lesions without preoperative FNA, 10 525 cases of FNA without histologic follow-up, and 16 456 cases of FNA with the histologic follow-up. On average, 44.2% +- 5.1% (mean +- [Standard Error*1.96]) of FNA cases proceeded to surgical resection. Results: ROM was estimated as 17%, 8%, 34%, 4%, 42%, 58%, and 91%, in nondiagnostic, nonneoplastic, atypia of undetermined significance, benign neoplasm, salivary gland neoplasm of uncertain malignant potential, suspicious for malignancy, and malignant groups, respectively. High level of heterogeneity was detected (P-value smaller 0.001	92 studies included, see article.	

number of FNA true and false positive, and true and false negative in comparison to histology cannot be reproduced based on the reported data, or the risk of malignancy (ROM) could not be separately determined for the intermediate and definite diagnostic categories.		including cases with definite fna diagnosis of neoplasm or malignancy summary estimates sensitivity specificity diagnostic odds ratio and positive negative likelihood in detecting neoplasms malignancies were respectively. metaregression showed several variables significantly impacting accuracy however subgroup analysis did not reduce the level heterogeneity. Author's Conclusion: FNA can be used as a reliable diagnostic tool in the preoperative evaluation and man-agement of salivary glands lesions. Concise of abstract is using Milan system for reporting salivarygland FNA could increase FNA reliability, facilitate communication, and improve patient care		
Methodical Notes				
Funding Sources: Not reported. COI: Authors have nothing to disclose. Study Quality: Two authors assessed the quality of the selected studies according to the Quality Assessment of Diagnostic Studies (QUADAS)-2 questionnaire to evaluate the risk of bias in the domains concerning the patient selection; index and reference test execution, evaluation, and interpretation; and study flow and timing. In the Deek's funnel plot asymmetry test; the regression coefficient between the DOR and the inverse of the root of the SE of DOR was −11.7 with a P-value: .001, suggesting the presence of significant publication bias. None of the studies were considered as low-bias-risk in all four domains. Heterogeneity: The Cochrane Q test showed significant heterogeneity in FNA sensitivity, specificity, and DOR (P-value <0.001). The I2 index of FNA				

sensitivity, specificity, and DOR were 70% (95% CI: 65%-76%), 74% (95% CI: 68%-82%), and 74% (66%-82%), respectively. Publication Bias: The presence of publication bias was assessed using the Deek's funnel plot asymmetry test. Visual asymmetry in the funnel plot and P-value smaller 0.1 for the slope coefficient could imply presence of publication bias Notes: Oxford level of evidence: 3 Systematic review and meta-analysis with consistently applied reference standard, blinding in some studies, predominantly retrospective studies and predominantly non-consecutively recruitment. Search details for date of final search not available, only English articles were searched. Inclusion criteria do not specify reference test. Presence of significant publication bias and heterogeneity limits implications of the analysis.	

Liu, C. C. et al. Sensitivity, Specificity, and Posttest Probability of Parotid Fine-Needle Aspiration: A Systematic Review and Meta-analysis. Otolaryngol Head Neck Surg. 154. 9-23. 2016

Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 3 Study type: Systematic review and meta-analysis of diagnostic studies (70 studies). To analyze the sensitivity and specificity of fine-needle aspiration (FNA) in distinguishing benign from malignant parotid disease. To determine the anticipated posttest probability of malignancy and probability of non-diagnostic and indeterminate cytology with parotid FNA. Databases: PubMed and Embase	Population: Adults and/or children presenting with clinically or radiographically identified parotid masses who subsequently underwent parotidectomy. Intervention: FNA was performed prior to surgery via palpation or ultrasound guidance. Comparison: Cytopathology results from the FNA as well as the histopathology results from the surgical specimen.	Primary: Diagnostic accuracy, true positives/negatives and false positives/negatives associated with FNA in diagnosing benign versus malignant disease; Secondary: - Results: Study overview: The systematic review yielded 70 criterion-meeting studies, 63 of which contained data that allowed for computation of numerical outcomes (n = 5647 patients; level 2a) and consideration of meta-analysis. Results: Subgroup analyses were performed in studies that were prospective, involved consecutive patients, described the FNA technique utilized, and	70 studies included. See article for list.	

Search period: (January 1, 1964, to November 1, 2014). Inclusion Criteria: 1. the study examined adults and/or children presenting with clinically or radiographically identified parotid masses who subsequently underwent parotidectomy; 2. FNA was performed prior to surgery via palpation or ultrasound guidance; 3. the cytopathology results from the FNA as well as the histopathology results from the surgical specimen are both reported; 4. the study denoted true positives/negatives and false positives/negatives associated with FNA in diagnosing benign versus malignant disease; and 5. the study was a randomized or quasi-randomized controlled trial, nonrandomized prospective trial, or retrospective review. Exclusion Criteria: 1. they did not contain sufficient data to determine the number of true positives/negatives and false		used ultrasound guidance. The I2 point estimate was >70% for all analyses, except within prospectively obtained and ultrasound-guided results. Among the prospective subgroup, the pooled analysis demonstrated a sensitivity of 0.882 (95% confidence interval [95% CI], 0.509–0.982) and a specificity of 0.995 (95% CI, 0.960–0.999). The probabilities of nondiagnostic and indeterminate cytology were 0.053 (95% CI, 0.030–0.075) and 0.147 (95% CI, 0.106–0.188), respectively. Author's Conclusion: FNA of the parotid gland has moderate sensitivity and high specificity in differentiating malignant from benign disease. Given the high positive LR, a positive FNA can predict the presence of malignancy with 98% to 100% accuracy, depending on the prevalence of malignancy. However, patients with a negative FNA may still have a tangible posttest probability of malignancy, particularly if the underlying prevalence of disease is high. Physicians should therefore take the pretest probability of malignancy in their patient populations into account when interpreting parotid FNA results. Significant heterogeneity was found among the included studies, particularly in terms of the classification and reporting of intermediate results. An effort to standardize the classification of parotid FNA findings would improve the		

positives/negatives; 2. they reported on salivary gland pathology as a whole, without distinguishing between parotid and other salivary glands; and 3. they were case reports or abstracts that did not contain sufficient data.		consistency with which surgeons interpret and approach intermediate results		
Methodical Notes				
Funding Sources: Funding source: None. COI: Declared, textbook royalties, universtity grants. See article Study Quality: Quality of studies was assesed, by the authors own criteria. Results are reported for individual studies. "Potential risks of bias were tracked. Specifically, we recorded whether the design of a study was prospective or retrospective, whether consecutive patients were described, whether blinding was employed, whether there was a technical description of the FNA method utilized, and whether FNAs were performed under ultrasound guidance." "The majority of studies had a retrospective or unspecified study design (91%) and involved nonconsecutive series of patients (72%)". Heterogeneity: The I2 statistic was used to evaluate heterogeneity among the included studies. It reflects the degree of variability that is due to more than chance alone. We used the following criteria to interpret the I2 statistic: 0%–40% indicates likely unimportant heterogeneity; 30%–60%, moderate heterogeneity; 50%–90%, significant heterogeneity; 75%–100%, considerable heterogeneity. For our pooled estimates, we present the associated I2 statistic along with its 95% confidence interval (CI). "Considerable heterogeneity was found among studies, with an I2 statistic of 72.4% (95% CI, 65.5%–79.3%) for sensitivity and 78.6% (95% CI, 73.6%–83.6%) for specificity." Publication Bias: The presence of publication bias was assessed by performing a Deeks' funnel plot asymmetry test. $P < .05$ was considered significant for the presence of bias. The overall symmetrical distribution of study estimates suggests that there is no publication bias. A P value of 0.341 supports the visual assessment.				

Notes: Oxford level of evidence: 3 Systematic review and meta-analysis of diagnostic studies without blinding, predominantly retrospective and nonconsecutive Considerable heterogeneity was found among studies, which limits implications.				
Novoa, E. et al. Role of ultrasound-guided core-needle biopsy in the assessment of head and neck lesions: a meta-analysis and systematic review of the literature. Head Neck. 34. 1497-503. 2012				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 2 Study type: Systematic review and meta-analysis of diagnostic studies (16 studies) To determine the role of CNB in the assessment of head and neck lesions Databases: Cochrane database of randomized controlled trials, PubMed/Medline Search period: Search period not specified. Inclusion Criteria: Only those publications that explicitly reported raw data, comparing the presumptive diagnosis of ultrasoundguided core needle biopsy in the head and neck with definitive histology obtained by excisional biopsy, were finally selected. In some instances, corresponding authors were contacted for patient data when specific information for statistical analysis was required.	Population: Patients with head and neck lesions. Intervention: Diagnosis of ultrasoundguided core needle biopsy Comparison: Definitive histology obtained by excisional biopsy	Primary: Diagnostic accuracy. Secondary: - Results: Study overview: A systematic review of the literature and meta-analysis of data extracted from 16 included studies were performed. A total of 1291 cervical lesions in 1267 patients were examined by CNB. This resulted in 1232 adequate samples, from which 554 were subsequently confirmed by excisional biopsy. Results: CNB was able to identify true neoplasms and detect malignancy in head and neck lesions with an overall accuracy of 94% and 96%, respectively, even though there was a significant difference between the histologically verified and all adequate samples. CNB provided a correct specific diagnosis in 87% of cases without major complications and achieved a higher accuracy than that of fine-needle aspiration in detecting malignancy	16 studies, of which 5 studied salivary glands. Buckland 1999, Howlet 2007, Kesse 2002, Taki 2005, Tang 2004	

Exclusion Criteria:		Author's Conclusion: This meta-analysis confirms that CNB is an excellent method in the assessment of salivary gland lesions and lymphadenopathies inclusive of malignant lymphoma, but it is not ideal for evaluating thyroid lesions.		
Methodical Notes				
Funding Sources: Not declared. COI: Not declared. Study Quality: Unclear, no evaluation of study quality was performed. Heterogeneity: No description or investigation. Publication Bias: No description or investigation. Notes: Oxford level of evidence: 2 systematic review and meta-analysis of diagnostic studies (retrospective and prospective) with consistently applied reference standard. Downgrade to evidence level 3. No assesment of study quality was performed. No investigation of heterogeneity, publication bias. No declaration of conflicts of interest. Only 5 out of 16 studies investigated salivary glands.				

1.5 Sammlung 03. Welche bildgebenden und klinischen Verfahren sind geeignet multifokale, benigne oder maligne Läsionen effektiv zu detektieren?

OXFORD (2011) Appraisal Sheet: Systematic Reviews

Bertagna, F. et al. Diagnostic role of (18)F-FDG-PET or PET/CT in salivary gland tumors: A systematic review. Rev Esp Med Nucl Imagen Mol. 34. 295-302. 2015				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 4 Study type: Systematic review of diagnostic studies (22 articles) To evaluate the diagnostic performance of PET in this particular setting,analyzing the available literature. Databases: PubMed/MEDLINE, Embase and Scopus including references of the retrieved articles Search period: Inception - 30th November 2014. Inclusion Criteria: Studies or subsets in studies investigating the role of 18F-FDG-PET or PET/CT in patients with SGTs. Exclusion Criteria: (a) articles not in the field of interest of this review; (b) review articles, editorials or letters, confer-ence proceedings; (c) case reports or small case series (<10patients). Only those	Population: Patients with salivary gland tumors. Intervention: 18F-FDG-PET or PET/CT Comparison: reference standard (not specifed).	Primary: Diagnostic accuracy. Secondary: - Results: 22 articles were included. The studies selected suggest that: (1) PET is not useful in discriminating benign frommalignant SGTs because of the overlap of uptake in both conditions; (2) PET not only is complementary toconventional imaging techniques for the staging and restaging but in some cases could also be superiorto them; (3) PET may often have a highly positive impact on clinical decision making. Author's Conclusion: Despite manylimitations affecting the analysis, PET seems to be useful in SGTs. However, more extensive studies and cost-effectiveness analyses are desirable to	22 studies are included, list see article.	

studies including whole-body18F-FDG-PETor PET/CT scans performed in patients with SGTs were included		determine its correct position in the diagnostic flow chart.		
Methodical Notes				
Funding Sources: Not disclosed. COI: The authors declare that they have no conflict of interest. Study Quality: Study quality was not assesed. Heterogeneity: No meta analysis was performed, due to high heterogeneity. Publication Bias: No investigated. Notes: Oxford level of evidence: 3 Systematic review of diagnostic studies with predominantly retrospective or unclear desing, unclear reference standard and no information regarding blinding or consecutive recruitment. Dwongrade to evidence level 4. Reference standard not specified. No meta-analysis was performed due to heterogeneity. The authors claim that this stems from differences in the reference standard. Study quality was not assesed.				

Kong, X. et al. The diagnostic role of ultrasonography, computed tomography, magnetic resonance imaging, positron emission tomography/computed tomography, and real-time elastography in the differentiation of benign and malignant salivary gland tumors: a meta-analysis. Oral Surg Oral Med Oral Pathol Oral Radiol. 128. 431-443.e1. 2019				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 2 Study type: Systematic review and meta-	Population: Patients with salivary gland tumors	Primary: Accuracy of differention between benign and malignant tumors	38 studies included, see	

analysis of diagnostic studies (38 studies) To assess the diagnostic properties of ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography/computed tomography (PET/CT), and real-time elastography (RTE) in distinguishing between benign and malignant salivary gland tumors Databases: PubMed, ScienceDirect, and Web of Science databases Search period: Inception - January 2019 Inclusion Criteria: (1) use of ultrasonography, CT, MRI, PET/CT, or RTE to differentiate benign from malignant salivary gland tumors; (2) comparison of the diagnostic results of the imaging modalities with a reference standard; and (3) provision of sufficient data for constructing 2£ 2 contingency tables. Exclusion Criteria: Citations that did not meet the aforementioned criteria, review studies, case reports, comments, unpublished materials, and studies published in abstract form were excluded.	Intervention: ultrasonography, CT, MRI, PET/CT, or RTE Comparison: reference standard (not specified)	Secondary: - Results: In total, 38 studies were included. Pooled sensitivities for ultrasonography, CT, MRI, PET/CT, and RTE were 0.66, 0.70, 0.80, 0.81, and 0.80, respectively. Pooled specificities were 0.92, 0.73, 0.90, 0.89, and 0.70, respectively. The DORs were 23, 6, 38, 20, and 10, respectively. The areas under the curve (AUC) of SROC for US, CT, MRI, PET/CT, and RTE were 0.91, 0.77, 0.92, 0.88, and 0.82, respectively. Author's Conclusion: Based on the results of the meta-analysis, MRI may be the first choice for the differential diagnosis of benign and malignant salivary gland tumors for its relatively high diagnostic value. PET/CT tends to have greater accuracy than CT. Ultrasonography and RTE may help achieve better diagnostic outcomes if they are used in conjunction.	article for list.	
Methodical Notes				
Funding Sources: This research is supported by Beijing Municipal Administration of Hospitals Incubating Program (code: PX2019057). COI: No declaration of conflcits of interest.				

Study Quality: The quality assessment of diagnostic accuracy study form (QUADAS-2) was used as the guideline. By judging 4 domains (patient selection, index test, reference standard, and flow and timing), each study was ranked as having high, unclear, or low risk of bias. According to the results of the QUADAS-2 items, high risk of bias was mostly observed in the "index test" category, other domains were low or unclear risk. Heterogeneity: Heterogeneity of each study group was tested using the x2 test and the inconsistency index (I2). An I2 greater than 50% and P value of the x2 test less than .05 confirmed the existence of significant heterogeneity, and a random effect model was chosen to pool the data. Otherwise, a fixed-effect model was used. High heterogeneity among the included studies was a major problem. Although meta-regression and subgroup analyses ruled out the influence of some factors on the study results, there were still other variances, such as patient demographic characteristics, specific devices used in evaluation, and cutoff values, which need to be considered. Publication Bias: Publication bias was analyzed by using the Deeks funnel plot and an asymmetry test. According to the Deeks funnel plot asymmetry test, no publication bias was detected among the studies in the ultrasonography (P =.87), CT (P = .84), MRI (P = .22), PET/CT (P = .69), or RTE (P = .98) groups. Notes: Oxford level of evidence: 2 Systematic review and meta-analysis of diagnostic studies with consistently applied reference standard; with blinding in some studies and both retrospective and retrospective study desgin (but with subgroup analysis for prospective/blinding) Reference not defined in inclusion criteria. No declaration of conflcits of interest. High heterogeneity limits implication.	

OXFORD (2011) Appraisal Sheet: Diagnostic Studies

Li, J. et al. Ultrasound and computed tomography features of primary acinic cell carcinoma in the parotid gland: a retrospective study. Eur J Radiol. 83. 1152-1156. 2014				
Evidence level/Study Types	Population	Outcomes/Results		
Evidence level: 4	Number of patients / samples: 117 consecutive patients with	Results: On US images, lesions were irregular, well-defined, hypoechoic, heterogeneous, and poorlyvascularized. On CT		

Study type: Retrospective diagnostic study without blinding but consistently applied reference standard. The aim of this study was to characterize the ultrasound (US) and computed tomography (CT) findings of primary acinic cell carcinoma (AciCC) of the parotid gland.	histopathologically proven primary solitary AciCC of the parotid gland who consulted our hospital between December 2003 and August 2012. Reference standard: The diagnosis of findings of primary acinic cell carcinoma (AciCC) was confirmed after surgical resection of the tumor and histological analysis of the tumor tissue. Validation: Ultrasound and computed tomography features Blinding: No blinding was performed. Inclusion of clinical information: - Dealing with ambiguous clinical findings: -	images, lesions were regular and well-defined, and showed slight heterogeneousenhancement. Detailed results see article. Author conclusions: The findings in this study suggest that the US features of mostprimary AciCCs are consistent with the CT features in terms ofthe border and echotexture or density on contrast scans; the only exception is tumor shape. Moreover, the findings indicate that mostprimary AciCCs show benign features on US and CT.		
Methodical Notes				
Funding Sources: This study was supported from the National Natural Science Foundation of China (No. 81272567). COI: None declared. Notes: Oxford level of evidence: 3 Retrospective diagnostic study without blinding but consistently applied reference standard. Downgrade to evidence level 4: CT and US were not available for all patients (only 13 out of 117 had data available for both US and CT), so direct comparison is limited. No blinding was performed. Retrospective evaluation more prone to selection bias.				

Mansour, N. et al. Multimodal Ultrasonographic Pathway of Parotid Gland Lesions. Ultraschall Med. 38. 166-173. 2017				
Evidence level/Study Types	Population	Outcomes/Results		
Evidence level: 3 Study type: Prospective diagnostic study.	Number of patients / samples: 202 patients with solitary circumscribed lesions of the parotid gland consulting the Department of Otorhinolaryngology of the Technische Universitaet Muenchen. Reference standard: All patients underwent surgical procedures meaning partial parotidectomy with a minimum free margin of 5mm, and definite histological examination. Validation: Pre-surgical high-resolution B-mode US, RTE, CDS, and CEUS. Blinding: no blinding was performed. Could have been possible for histology. Inclusion of clinical information: Yes. Medical history, clinical examination available for all patients. Dealing with ambiguous clinical findings: -	Results: Histology revealed 170 benign and 32 malignant PLs. Medical history, clinical examination, and B-mode US identified malignancy with a sensitivity/specificity of 77 %/98 %. After application of CDS and CEUS in the multimodal pathway, the sensitivity of malignant tumors increased to 91 %. The decreased specificity (81 %) was equalized by intraoperative frozen section (PPV 48 %, NPV 98 %). After application of the multimodal pathway, only 1 patient underwent repeat surgery. Author conclusions: The multimodal ultrasonographic pathway reliably identifies malignant parotid gland lesions to provide uncertain resection margins, repeat surgery, and therefore, higher risk for facial palsy. By augmenting the multimodal ultrasonographic pathway, maybe the specificity and positive predictive value of malignant parotid gland lesions and the sensitivity of pleomorphic adenomas and Warthin's tumors can be increased.		
Methodical Notes				

Funding Sources: not declared. COI: The authors declare that they have no conflict of interest. Notes: Oxford level of evidence: 3 prospective diagnostic study with consistently applied reference standard, but not blinding. Reference standard was applied regardless of the results of the index test, but was not blinded.		

1.6 Sammlung 04. Welche diagnostischen Verfahren eignen sich bei der Identifikation von nicht-speicheldrüseneigenen Tumoren?

OXFORD (2011) Appraisal Sheet: Systematic Reviews

Haldrup, M. et al. Utility of ultrasound of the lymph nodes in patients with high-risk cutaneous squamous cell carcinoma. European Journal of Plastic Surgery. 41. 619-624. 2018				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 3 Study type: Systematic review of diganostic studies with consistently applied reference standard but not blinding. (8 studies) To evaluate ultrasound in the diagnostics of lymph node metastases in cutaneous squamous cell carcinoma and in the light of different Bhigh-risk^ factors in cSCC to evaluate who would benefit from US. Databases: PubMed, Embase and Cochrane Search period: 2000 until September 2017. Inclusion Criteria: Studies containing information about US used for examination of lymph nodes of the neck in HNSCC were included. Further, only articles based on histologically evaluated pathology of the lymph nodes were included. Histologically	Population: Patients with squamous cell carcinoma of the head neck (HNSCC) Intervention: US Comparison: CT, PET CT	Primary: Sensitivity, specificity and negative predictive value (NPV) were calculated for each study and a cumulative calculation was made Secondary: - Results: Sensitivity for US for the total cohort was 85.9, specificity was 96.3%, negative predictive value (NPV) was 93.1% and accuracy was 92.2%. We found significantly no difference when US was compared to CT and PET CT. CT had a sensitivity, specificity, NPV and accuracy at 82.8, 97.7, 90.9 and 92.32%respectively. Sensitivity, specificity, NPVand accuracy for PET CT were 87.4, 98.1, 95.2 and 95.2% respectively. In contrast,we found clinical examination to have the significantly lowest sensitivity, specificity, NPV and accuracy at 69.6, 80, 61.1 and 73.4%, respectively.	8 studies included: total n = 664 Souren et al. 2016, Safaan et al. 2013, Stoeckli et al. 2011, Yoon et al. 2009, Akoglu et al. 2005, Thomasen et al. 2005, Haberal et al. 2004, Jank et al. 2002, Stukesen et al. 2002	

examination was considered gold standard in all included articles. Lastly, articles included had to contain information on sensitivity and specificity for US from the lymph nodes. Patients in the different included studies were selected for undergoing US (and different other modalities varying in the studies) if they had a previously untreated, histology proven SCC of the head and neck Exclusion Criteria: Casuistic studies and studies that did not differentiate between cSCC of the head and neck and the rest of the body were excluded.		Author's Conclusion: Ultrasound is found to have equal sensitivity, specificity and NPV as CT and PET CT. Further, US is proven significant better than clinical examination. Patients with one or two high-risk factors for metastases could very well benefit from US of neck. However, more studies on US are necessary and further, specific studies on cSCC should be performed in order to see if US of the neck in HNSCC patients is transferable to cSCC. Level of evidence: Not ratable.		
Methodical Notes				
Funding Sources: not declared. COI: Declared, none present. Study Quality: No evaluation of study quality. Heterogeneity: No meta-analysis was performed. Publication Bias: Less than 10 studies were included, No meta-analysis was performed. Notes: Oxford level of evidence: 2 Systematic review of diagnostic studies without consistently with consistently applied reference standard, but not blinding or information regarding consecutive recruitment. Downgraded to evidence level 3 due to poor quality.				

No search for grey literature. Only English literature was searched. Unclear if selection or data extraction were carried out by more than one investigator. No evaluation of study quality.	

OXFORD (2011) Appraisal Sheet: Diagnostic Studies

Akbas, Y. et al. Ultrasonography guided fine needle aspiration biopsy of parotid gland masses. Kulak Burun Bogaz Ihtis Derg. 13. 15-8. 2004				
Evidence level/Study Types	Population	Outcomes/Results		
Evidence level: 3 Study type: Diagnostic study (likely retrospective design) US guided FNA vs histopathology of parotid gland masses before surgery.	Number of patients / samples: 46 female and 36 male patients with parotid gland masses. Reference standard: Histopathology was applied to all samples, regardless of index test results. Validation: Index test was US guided FNA. Blinding: No blinding was performed. Inclusion of clinical information: - Dealing with ambiguous clinical findings: -	Results: "In our series 65 (79%) of the lesions were found to be benign and 17 (21%) malignant. There were one false negative and one false positive result. The sensitivity, specifity and accuracy rates are found to be 94.1%, 98.4% and 97.6% for parotid tumors, respectively." Author conclusions: "Ultrasonography guided fine needle aspiration biopsy of parotid gland masses have been proven to be a highly specific, sensitive and a safe preoperative diagnostic technique when performed by an experienced clinician and cytopathologist."		
Methodical Notes				
Funding Sources: not stated. COI: not stated.				

Notes: Oxford level of evidence: 3 retrospective diagnostics study with consistently applied reference standard without blinding. No declaration of potential conflicts of interest.				
Aro, K. et al. An evaluation of the diagnostic methods in head and neck cancer of unknown primary site. Acta Oto-Laryngologica. 138. 930-936. 2018				
Evidence level/Study Types	Population	Outcomes/Results		
Evidence level: 3 Study type: Retrospective analysis of patients with head and neck cancer of unknown primary (HN-CUP). Comparison of various detection methods to identify the primary tumor and to improve and standardize management.	Number of patients / samples: Patients with with HN-CUP at the Helsinki University Hospital during 1995–2011. Reference standard: Not applicable: Clinical assessment, definitive treatment, histopathology, and follow up were evaluated. Validation: - Blinding: No blinding was performed. Inclusion of clinical information: - Dealing with ambiguous clinical findings: -	Results: Frequency of HN-CUP and success in identifying the primary site have remained constant despite the addition of PET-CT and determination of human papilloma virus (HPV) status in diagnostics. Among 133 patients, the diagnostic work up identified the primary site in 53% and the oropharynx predominated (69%). This left 85 patients with HN-CUP and 5-year overall and disease-free survival rates were 71 and 69%, respectively. Author conclusions: Panendoscopy including tonsillectomy should not be omitted in the work up. We demonstrate a steady frequency of HN-CUP and constant success in identifying the primary site. Detection of a primary later in the follow up did not impact the survival.		
Methodical Notes				

Funding Sources: This study was funded by the Sigrid Juselius Foundation, the Finnish Otorhinolaryngology Research Foundation, and the Helsinki University Hospital Research Funds COI: No potential conflict of interest was reported by the authors. Notes: Oxford level of evidence: 3 Retrospective cohort analysis without blinding or consistently used reference standard.		

Celebi, I. et al. Quantitative diffusion-weighted magnetic resonance imaging in the evaluation of parotid gland masses: A study with histopathological correlation. Clinical Imaging. 37. 232-238. 2013				
Evidence level/Study Types	Population	Outcomes/Results		
Evidence level: 3 Study type: Diagnostic study (not specified, likely retrospective). (DW-MRI) vs histology in evaluation of parotid gland masses.	Number of patients / samples: 75 patients with 81 parotid gland masses Reference standard: Histology was applied in all cases, regardless of the outcome. Validation: Index test was DW-MRI. Blinding: Blinding was not performed. Inclusion of clinical information: age.	Results: Study overview: 75 patients ranged in age from 10 to 83 years: 36 were male and 39 were female, with mean ages of 44.8±18.8 and 49.4±13.0 years, respectively. Of the 81 masses, 49 (60.5%) were diagnosed as benign lesions, while 32 (39.5%) were diagnosed as malignant lesions. Diagnoses see article. Results: DW-MRI ADC values for distinguishing between malignant and benign parotid tumors The mean ADC values of the 49 benign tumors 1.72×10−3 mm2/s) were significantly higher than those of the 32 malignant tumors (1.05×10−3 mm2/s). No significant association was found between the malignancy status of the tumor and the gender of the patients. The mean age of patients with malignant tumors was significantly higher (51.75 years) than that of patients with benign tumors (43.93 years). We attempted to define a cutoff value for ADC values to distinguish between malignant and benign tumors through ROC analysis. Our analysis revealed that an ADC value of 1.165 would be a plausible cutoff point for optimizing the sensitivity and specificity of DW-MRI for distinguishing between the malignancy status of parotid tumors with sensitivity, specificity, and positive and negative predictive		

	Dealing with ambiguous clinical findings: -	value of 63.3%, 71.9%, 79%, and 79%, respectively. DW-MRI ADC values for distinguishing among tumor types: The highest mean ADC values were observed for the 28 pleomorphic adenomas (2.15±0.298×10−3 mm2/s), while the lowest ADC scores were observed for the five adenoid cystic carcinomas (0.84×10−3 mm2/s) and the two acinic cell carcinomas (0.89×10−3 mm2/s). The ADC scores for the Warthin tumors, lymphomas, adenoid cystic carcinomas, and mucoepidermoid carcinomas were 0.91×10− 3, 0.98×10−3, 0.84×10−3, and 1.27×10−3 mm2/s, respectively. Among the malignant tumors, the highest mean ADC value was for the six mucoepidermoid carcinomas. Author conclusions: "In conclusion, the results of our study showed that DWI may be useful for distinguishing between pleomorphic adenomas and other parotid masses, particularly malignant tumors. The diagnostic value of DWI would increase when routine MRI sequences are applied in combination with morphological analyses. Differentiation of lesions would be very helpful with respect to the surgical approach. However, the primary role of radiological imaging is currently limited in determining the localization, size, and morphology of lesions."		
Methodical Notes				
Funding Sources: Not declared. COI: Not declared. Notes: Oxford level of evidence 3: Retrospective study with consistently applied reference standard but without blinding. Uncear aim or description of outcomes. Lack of blinding.				
Hung, D. S. W. et al. Ultrasound-guided versus free-hand fine-needle aspiration cytology of the parotid gland: A single-centre, retrospective review. Surgical Practice. 22. 111-115. 2018				
Evidence level/Study Types	Population	Outcomes/Results		

Evidence level: 3 Study type: Retrospective study design. "To evaluate the accuracy and yield of free-hand FNAC versus ultrasound-guided FNAC and its subsequent correlation to the final pathology in order to evaluate its use as a preoperative investigational tool."	Number of patients / samples: 155 Patients who underwent in the Queen Elizabeth Hospital, Hong Kong, by the general surgical team during between 1 January 2008 and 31 March 2016. Reference standard: free-hand FNAC and histopathological diagnosis Validation: Ultrasound-guided FNAC and histopathological diagnosis Blinding: No blinding was performed. Inclusion of clinical information: not reported. Dealing with ambiguous clinical findings: not reported.	Results: Ultrasound-guided FNAC had 100 per cent specificity, whereas free-hand FNAC had 98.3 per cent specificity for detecting malignancy. Sensitivity was 92.9 per cent in the ultrasound-guided FNAC group versus 90 per cent in the free-hand FNAC group. Ultrasound-guided FNAC offered a preoperative diagnosis as to whether a mass was benign or malignant in 21 out of 75 patients (28 per cent), while free-hand FNAC was able to do so in 15 out of 80 patients (18.8 per cent). However, this was not statistically significant (P = 0.188). Author conclusions: Overall, both ultrasound-guided and free-hand FNAC have high sensitivity and specificity for diagnosing malignancy preoperatively. Free-hand FNAC does not have a lower yield and was not shown to be statistically inferior to ultrasound-guided FNAC. Free-hand FNAC is a good alternative in certain cases where the parotid lesion can be easily accessible.		
Methodical Notes				
Funding Sources: not disclosed. COI: "The authors report no conflicts of interest" Notes: Oxford level of evidence: Retrospective diagnostic study with consistently applied reference standard without blinding.				
Kraft, M. et al. Evaluation of clinician-operated sonography and fine-needle aspiration in the assessment of salivary gland tumours. Clin Otolaryngol. 33. 18-24. 2008				

Evidence level/Study Types	Population	Outcomes/Results		
Evidence level: 4 Study type: Retrsopective case review. US + FNA vs histopathology in salivary gland massses.	Number of patients / samples: One hundred and three patients with a total of 106 focal masses of the salivary glands were included. Reference standard: Histopathology was not applied in all cases. Validation: Index test was comnbination of US + FNA. Blinding: No bliding was performed. "The otolaryngologists were not blinded to the results of CT and MRI at the time of US, and the radiologists were supplied with previous findings of sonography and FNA." Inclusion of clinical information: - Dealing with ambiguous clinical findings: -	Results: The combination of US + FNA achieved a diagnostic accuracy of 99% in identifying and differentiating true salivary gland neoplasms from tumour-like lesions. In detecting malignancy, this combination permitted an accuracy of 98%. An approximate diagnosis was possible in 89%, and a specific diagnosis in 69% of our patients. Author conclusions: "Due to economic factors and a high diagnostic accuracy, the combination of US + FNA represents the investigation method of choice for most salivary gland tumours. We suggest that the otolaryngologist be employed in carrying out these procedures, as is already the rule in other medical specialties, while computed tomography and magnetic resonance imaging should be reserved to those few lesions, which cannot be delineated completely by sonography."		
Methodical Notes				
Funding Sources: not described. COI: None to declare. Notes: Oxford level of evidence: 4 retrospective study without consistently applied reference standard or blinding.				

Milad, P. et al. The added value of pretreatment DW MRI in characterization of salivary glands pathologies. Am J Otolaryngol. 38. 13-20. 2017				
Evidence level/Study Types	Population	Outcomes/Results		
Evidence level: 2 Study type: Prospective diagnostic study. Comparison of DW-MRI with ADC and histology prior to surgery.	Number of patients / samples: 46 patients, likely representative. Reference standard: Histology was applied for all patients regardless of index test results. Validation: Index test was DW-MRI with apparent diffusion coefficient (ADC) Blinding: Yes. "A consultant radiologist reviewed the scans to comment on the ADC value and ADC histogram. He was blind to the suspected pathology." Inclusion of clinical information: sex ,smoking habits between the groups. Dealing with ambiguous clinical findings: -	Results: Study population: 46 patients were included; 15 (33%) were males and 31 (67%) were females;age ranged from 21 to 67 years (mean 49.8±11.3). The final histopathology of the salivary gland lesions was benign in 25 cases (54%), and malignant in 21 cases (46%). See article for list. Results: The ADC values of all cases ranged from 2.6x10-3mm2/s to 0.4x10-3mm2/s (mean 1.27x10-3mm2/s ±0.55). There was an insignificant difference in ADC value across the various benign lesions. The highest ADC value was in patients with parotid pleomorphic adenoma (2.6x10-3mm2/s), whereas the lowest ADC value was seen in a patient with parotid non hodgkin lymphoma (0.4x10-3mm2/s). There was no significant difference in ADC value across the various malignant lesions .The mean ADC value for the benign lesions was 1.67x10-3mm2/s (±0.42),while that for malignant lesion was 0.8x10-3mm2/s(±0.18) (figure 4). There was no significant difference regarding sex ,smoking habits between the groups. Age distribution, and ADC values were significantly different (p=0.003 and p=0.0001, respectively). Using ROC curve analysis, an ADC value of ≤1.1 x10-3mm2/s was found to be a plausible cutoff point to differentiate benign from malignant lesions. Accordingly, all cases were properly diagnosed, except for one case with parotid Warthin tumor which was misinterpreted as malignant lesion, as its ADC was 0.8x10-3mm2/s. The diagnostic performance of DW-MRI for identification of malignant lesions showed that the sensitivity, specificity, PPV, and NPV were 100%, 92%, 91.3%, and 100%, respectively.		

		Author conclusions: In conclusion, the specific ability of DW-MRI to probe tissue microstructures is an interesting complement to the currently used imaging procedures in the characterization, and even grading of malignancies. ADC mapping is an easy, cost effective promising tool that has neither radiation exposure, nor amalgam artifacts and can be used in helping characterization of salivary glands lesions.		
Methodical Notes				
Funding Sources: None COI: None Notes: Oxford level of evidence: 2 Individual cross sectional studies with consistently applied reference standard and blinding. Outcomes lack description.				
Wang, P. et al. Lymphoepithelial carcinoma of salivary glands: CT and MR imaging findings. Dentomaxillofac Radiol. 46. 20170053. 2017				
Evidence level/Study Types	Population	Outcomes/Results		
Evidence level: 3 Study type: Retrospective diagnostic study without blinding, but with consistently applied reference standard	Number of patients / samples: 103 salivary gland LEC (lymphoepithelial carcinoma) patients. Reference standard: surgical treatment and histopathological examination Validation: CT and MRI	Results: Based on the pathological outcomes, all the salivary gland LECs were classified into two types from CT and MRI scans: solitary LEC (56 cases, 54.4%) and multiple LEC (47 cases, 45.6%). The latter included solitary salivary gland LEC with extraglandular lymphnode metastases (12 cases), parotid gland LEC with ipsilateral intraglandular lymph-node metastases (11 cases), parotid gland LEC with ipsilateral intra- and extraglandular lymphnode metastases (23 cases) and bilateral parotid gland LEC (1 case). The salivary gland LEC was depicted on CT and MRI scans as a lobular mass in 64 of 104 (61.5%), homogeneous mass in 65 of 104 (62.5%) or enhanced neoplasm in 94 of 104 (90.4%).		

	Blinding: No blinding was performed. Inclusion of clinical information: not reported. Dealing with ambiguous clinical findings: not reported.	Author conclusions: Salivary gland LEC has a predilection for females in the fourth to fifth decade of life and the parotid gland. CT and MRI findings between solitary and multiple salivary LECs vary. A majority of multiple parotid gland LECs are characterized by metastasis of ipsilateral intraglandular lymph nodes, which may accompany with or without extraglandular lymph-node metastases		
Methodical Notes				
Funding Sources: not declared. COI: not declared. Notes: Oxford level of evidence: 3 Retrospective diagnostic study without blinding, but with consistently applied reference standard. No declaration of funding or potential conflicts of interest. No blinding was performed.				

1.7 Sammlung 05. Welches chirurgische Verfahren ist bei gutartigen Tumoren der Glandula parotis effektiv?

OXFORD (2011) Appraisal Sheet: Systematic Reviews

Albergotti, W. G. et al. Extracapsular dissection for benign parotid tumors: a meta-analysis. Laryngoscope. 122. 1954-60. 2012				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 4	Population: Patient with clinically benign parotid	Primary: Recurrence, facial weakness, Frey's syndrome	Glaeve 1979, Martis 1983, Prichard	

Study type: Systematic literature review and meta-analysis of mostly retrospective cohort studies. (9 studies) Study investigates complication rates and effectiveness of ECD versus superficial parotidectomy (SP) for the treatment of primary benign parotid neoplasms. Databases: Ovid/Medline Search period: not defined Inclusion Criteria: Studies that compared ECD to SP with regard to at least one outcome of interest (recurrence, facial weakness, Frey's syndrome) in the surgical management of solitary, clinically benign parotid nodules. Exclusion Criteria: Studies were excluded if they included recurrent or multiple tumors where the data could not be separated from primary, solitary tumors, involved nonparotid salivary tumors, or included malignant neoplasms.	nodules. Intervention: ECD: defined by capsular dissection of the tumor with a thin margin of surrounding gland without planned identification of the main trunk of the facial nerve. Comparison: SP: defined as both complete and partial SP, where a portion of the superficial lobe is removed with the tumor after planned identification and dissection of the facial nerve.	Secondary: - Results: The included studies evaluated a total of 1,882 patients. There was no observed difference in tumor recurrence between the ECD and SP groups (odds ratio [OR], 0.557; 95% confidence interval [CI], 0.271-1.147). There was a significantly lower rate of transient facial nerve paresis (OR, 0.256; 95% CI, 0.174-0.377) in the ECD group (59 of 741; 8.0%) compared to the SP group (81 of 397; 20.4%); however, there was no observed difference in permanent facial paralysis between the ECD and SP groups (OR, 0.878; 95% CI, 0.282-2.730). Frey's syndrome was less often observed (OR, 0.117; 95% CI, 0.071-0.191) after ECD (27 of 602; 4.5%) compared to SP (75 of 287; 26.1%). Author's Conclusion: This systematic review with meta-analysis suggests that ECD has a similar recurrence rate as SP with fewer postoperative complications. ECD may be considered an alternative surgical modality for select benign parotid neoplasms.	1992, Natvig & Soberg 1994, Hancock 1999, Marti 2000, Witt 2003, McGurk 2003, Uyar 2011,	
Methodical Notes				
Funding Sources: The authors have no funding, financial relationships, or conflicts of interest to disclose.				

COI: The authors have no funding, financial relationships, or conflicts of interest to disclose. Study Quality: Not investigated. Heterogeneity: The Q value, a measure of the heterogeneity of the included studies, tested the null hypothesis that the studies are homogeneous. If the test of heterogeneity was statistically significant (P < .05), then more emphasis would have to be placed on the random-effects model. Publication Bias: Not applicable, less than 10 studies investigated. Notes: Oxford level of evidence: 3 Systematic literature review and meta-analysis of retrospective cohort studies. Downgrade to evidence level 4 Only one database was searched. No timeframe for the search was provided. No search for grey literature. Articles were not selected and extracted by two reviewers. No evaluation of study quality. No heterogeneity outcomes presented.	

Foresta, E. et al. Pleomorphic adenoma and benign parotid tumors: extracapsular dissection vs superficial parotidectomy--review of literature and meta-analysis. Oral Surg Oral Med Oral Pathol Oral Radiol. 117. 663-76. 2014

Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 3 Study type: Systematic review and meta-analysis (19 studies) This study compared extracapsular dissection (ED) vs superficial parotidectomy (SP) in the treatment of pleomorphic adenoma and benign parotid tumors Databases: PubMed, Ovid	Population: Patients with primary tumor (pleomorphic adenoma) in the superficial lobe, size: less than 4 cm, no involvement of cranial nerve VII, unifocal, unilateral, capsular integrity Intervention: Extracapsular dissection (ED) Comparison: Superficial parotidectomy (SP)	Primary: Recurrence, permanent facial nerve paralysis, Frey syndrome. Secondary: - Results: 19 studies were included. Pleomorphic adenoma recurrence pooled incidence rates were analyzed, excluding studies with a follow-up of less than 5 years. The recurrence appeared to be more common among patients with indication for superficial parotidectomy (pooled	16 studies included: chan 2010, Ghosh 2003, Guntinas 2004, Guntinas 2006, Hancock 1999, Henriksson 1998, Laskawi 1996, Leverstein 1997, McGurk 1996, McGurk 2003 Natvig 1994, O'Brien 2003, Piekarski 2004, Prichard 1992, Riad 2011, Shehata 2010, Smith 2007,	

MEDLINE, the Cochrane Database of Systematic Reviews, and Scopus from Search period: 1950 to 2011. Inclusion Criteria: English articles, ≥ participants, Age range (y) 18-65, Follow-up 12 months. Patients with Primary tumor Superficial lobe , size: less than 4 cm, no involvement of cranial nerve VII, unifocal, unilateral, capsular integrity. Exclusion Criteria: -		incidence rate, 2.0 cases per 1000 person-years; 95% CI, 0.9-3.6) compared with patients who underwent extracapsular dissection (1.3 cases per 1000 person-years; 95% CI, 0.4-2.9), and these results were consistent with the observations on all benign tumors (pooled incidence rate for extracapsular dissection, 0.2 cases per 1000 person-years; 95% CI, 0.1-0.8; pooled incidence rate for superficial parotidectomy, 2.3 cases per 1000 person-years; 95% CI, 1.0-4.1). Patients who underwent extracapsular dissection experienced fewer cases of total paralysis (pooled proportion, 1.1%; 95% CI, 0.3%-2.6%) compared with those who underwent superficial parotidectomy (2.2%; 95% CI, 0.4%-5.3%). Also, Frey syndrome was less common in patients who underwent extracapsular dissection (5.0%; 95% CI, 3.0%-7.0% vs 28%; 95% CI, 13.0%-46.0%). All these results were somewhat consistent with the outcomes observed in the all-benign-tumors population. Author's Conclusion: We may conclude that in patients with unilateral pleomorphic adenoma, located in the superficial lobe, sized less than 4 cm and with no clinical involvement of cranial nerve VII, extracapsular dissection represents a	Takahama 2009, Van Niekerk 1987.	

		viable alternative option to superficial parotidectomy in terms of successful outcome, convenience, and ease of performance. These findings are consistent with results obtained from the evaluation of all benign tumors. On the other hand, extracapsular dissection should not be considered in cases involving sizable tumors with poor mobility (≥4 cm), malignant histology, or parotid deep lobe involvement.		
Methodical Notes				
Funding Sources: not declared. COI: not declared. Study Quality: No assesment of study quality. Heterogeneity: Not investigated. Publication Bias: Publication bias not investigated, but not feasible with less than 10 studies per analysis. Notes: Oxford level of evidence: 2 Systematic review and meta-analysis of retrospective cohort studies. Downgrade to evidence level 3 No declaration of potential conflicts of interest or funding. No assesment of study quality or heterogeneity. The last searches were performed sometime in 2011, while the article was published in 2014, an update search could have been performed while it was in the making.				

Lin, Y. Q. et al. Extracapsular dissection versus partial superficial parotidectomy for the treatment of benign parotid tumours. International Journal of Oral and Maxillofacial Surgery. 48. 895-901. 2019				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 3 Study type: Systematic Review and Meta-Analysis of Cohort studies: Six retrospective, one prospective (1641 patients included) To compare the complications of patients treated for a benign parotid tumour (BPT) by extracapsular dissection (ECD) vs. partial superficial parotidectomy (PSP) Databases: PubMed and Cochrane Library Search period: Inception to September 2018 Inclusion Criteria: Studies comparing ECD and PSP in patients undergoing surgery for BPTs with an accurate description of the surgical technique and reporting at least one quantitative	Population: Patients undergoing surgery for benign parotid tumour (BPTs) Intervention: Extracapsular dissection (ECD) Comparison: Partial superficial parotidectomy (PSP)	Primary: Facial nerve injury, Frey syndrome, recurrence, infections, Salivary fistula or sialocele Secondary: Results: A total of 1641 patients from seven studies (1120 ECDtreated and 521 PSP-treated patients) were included in this meta-analysis. Transient facial nerve injury (odds ratio (OR) = 0.28, 95% confidence interval (CI): 0.11– 0.71; p = 0.008) and Frey syndrome (OR = 0.12, 95% CI: 0.03–0.48; p = 0.003) were less prevalent in the ECD group. The rates of permanent facial nerve injury (OR = 0.77, 95% CI: 0.35–1.70; p = 0.520), recurrence rate (OR = 0.17, 95% CI: 0.02–1.75; p = 0.14), infection (OR = 0.70, 95% CI: 0.07–6.67; p = 0.76), and salivary fistula/sialocele (OR = 0.40, 95% CI: 0.06–2.66; p = 0.350) were similar in both groups. Author's Conclusion: In conclusion, this meta-analysis assessed the best evidence available for guiding clinical decisions regarding BPT resection, with the aim of minimizing complications. The results of this metaanalysis favoured ECD, which conserves more tissue than	7 studies (1641 participants) included: Witt 2012, Zheng 2018, Mantsopoulos 2015, Iro 2013, Ciuman 2012, Park 2018, Wong 2017	

outcome measure were included Exclusion Criteria: The exclusion criteria were parotid malignancy, case reports/review articles, and lack of a stated follow-up period.		PSP, thereby reducing the occurrence of complications. Because the level of the clinician's experience may influence the outcomes of BPT treatment, we recommend that these operations be performed selectively by experienced surgeons. Future well-designed, randomized clinical trials with a large number of patients and an extensive follow-up period are needed to confirm and update the findings of this analysis.		
Methodical Notes				
Funding Sources: None. COI: None. Study Quality: Study quality was assessed with the Newcastle–Ottawa Scale. The quality of the included studies was generally low. None of the retrospective studies provided an appropriate protocol for treatment assignment, and the patients were allocated into the treatment groups by clinicians. In most studies included in this metaanalysis, the methods used for handling missing data and intention-to-treat analyses were not explicitly defined Heterogeneity: Inter-group heterogeneity was assessed with x2 and I2 statistics, which are reported with degrees of freedom (df). Facial nerve injury: No significant between-study heterogeneity (x2 = 0.80, df = 2, p = 0.670; I 2 = 0%), Frey syndrome: There was no significant between-study heterogeneity (x2 = 3.07, df = 2, p = 0.220; I 2 = 35%), Recurrence: No significant betweenstudy heterogeneity (x2 = 0.39, df = 1, p = 0.53; I 2 = 0%) Publication Bias: Begg's test and funnel plot analyses were used to detect publication bias.A two-tailed $p < 0.05$ was considered significant. No publication bias was detected (Begg's test, p = 0.373 Notes: Oxford CEBM Level of Evidence 2011: EL 3 Systematic Review and Meta-Analysis of retrospective and prospective studies				

-Overall quality of the included studies was low -No search for grey literature or unpublished studies was conducted	

NEWCASTLE - OTTAWA Checklist: Cohort

<table>
<tr><td colspan="4">Stathopoulos, P. et al. Partial Superficial, Superficial, and Total Parotidectomy in the Management of Benign Parotid Gland Tumors: A 10-Year Prospective Study of 205 Patients. Journal of Oral and Maxillofacial Surgery. 76. 455-459. 2018</td></tr>
<tr><td>Study type</td><td>Methodical Notes</td><td>Patient characteristics</td><td>Interventions</td></tr>
<tr><td>Evidence level:
3
Study type:
Prospective cohort study with consecutive recruitment.
To present an overview of our experience in treating parotid gland tumours over a period of 10 years.</td><td>Funding sources:
No funding was used.

Conflict of Interests:
No conflict of interest.

Randomization:
-

Blinding:
-

Dropout rates:
-</td><td>Total no. patients:
205 consecutive patients with a variety of parotid gland tumours who underwent surgery at Northampton General Hospital

Recruiting Phase:
October 2000 to November 2010.

Inclusion criteria:
Consecutive inclusion of patients with a variety of parotid gland tumours who underwent surgery.

Exclusion criteria:
-</td><td>Interventions:
partial superficial parotidectomy

Comparison:
superficial parotidectomy</td></tr>
<tr><td>Notes:</td><td colspan="3">Oxford level of evidence: 3 Prospective cohort study with consecutive recruitment

Author's conclusion:
As a risk or recurrence is higher when surgery is performed by non-experienced surgeons we advocate that parotid gland surgery should be performed by adequately trained operators and the surgical specimen should ideally be examined by a histopathologist experienced in the diagnosis of salivary gland tumours. Recurrence rate for these tumours increases with time therefore a long term follow up is required for these patients</td></tr>
<tr><td>Outcome Measures/results</td><td>Primary
Surgical outcomes:</td><td colspan="2">Results:
Our study confirmed that good results in terms of low recurrence rate and minimal risk</td></tr>
</table>

	Recureence rate, facial nerve damage. Secondary -	of facial nerve weakness can be achieved with operations less aggressive than the traditional superficial parotidectomy, such as partial superficial parotidectomy. Transient facial nerve palsy was significantly more frequent after total (40%, p<0.001) and superficial parotidectomy (28%, p< 0.05), respectively, than after partial superficial parotidectomy (9.6%).

1.8 Sammlung 06. Welches chirurgische Verfahren ist bei gutartigen Tumoren der kleinen Speicheldrüsen und den Gll. submandibulares et sublinguales effektiv?

NEWCASTLE - OTTAWA Checklist: Cohort

<table>
<tr><td colspan="4">Yang, T. L. Robotic surgery for submandibular gland resection through a trans-hairline approach: The first human series and comparison with applicable approaches. Head and Neck. 40. 793-800. 2018</td></tr>
<tr><td>Study type</td><td>Methodical Notes</td><td>Patient characteristics</td><td>Interventions</td></tr>
<tr><td>Evidence level:
3
Study type:
Prospective cohort study
We confirm the feasibility and safety of applying robotic surgery through a trans-hairline approach for comprehensive submandibular gland surgery in the first human series</td><td>Funding sources:
Not stated

Conflict of Interests:
Not stated

Randomization:

Blinding:

Dropout rates:</td><td>Total no. patients:
24

Recruiting Phase:
From 2012 to 2017

Inclusion criteria:
Patients who were diagnosed with submandibular gland diseases and scheduled for robotic surgery

Exclusion criteria:
The patients were excluded from the study if they had previous neck surgery or irradiation, contraindication for surgery or general anesthesia, submandibular gland diseases with extraglandular extension, or submandibular gland malignancy with potential extensive cervical metastases</td><td>Interventions:
Robotic submandibular gland resection through the trans-hairline approach

Comparison:</td></tr>
<tr><td>Notes:</td><td colspan="3">Oxford CEBM Level of Evidence 2011: EL 3 Cohort Study
-Feasibility study
-Overall, the number of included patients is very small. Therefore the implication if this article for practice is</td></tr>
</table>

	limited. -No comparison group -Conflict of interest and funding was not described Author's conclusion: This study demonstrated the feasibility and safety of the trans-hairline approach for robotic submandibular gland resection in the first human series. The procedure is applicable to many submandibular gland diseases with complete disease control, and has aesthetic advantages over other robotic surgical approaches.	
Outcome Measures/results	Primary Postoperative aesthetic satisfaction Secondary	Results: All surgical procedures were successfully performed without conversion and appreciable complications. The incision was completely concealed within the hairs. Treatments of submandibular gland benign or malignant tumors were completed without any positive margins or disease recurrence.

1.9 Sammlung 07. Welches chirurgische Verfahren ist bei bösartigen Tumoren der großen Speicheldrüsen zur lokalen Tumorkontrolle effektiv?

NEWCASTLE - OTTAWA Checklist: Cohort

<table>
<tr><td colspan="4">Israel, Y. et al. Diagnostic and therapeutic modalities for 287 malignant and benign salivary tumors: A cohort study. J Craniomaxillofac Surg. 45. 585-588. 2017</td></tr>
<tr><td>Study type</td><td>Methodical Notes</td><td>Patient characteristics</td><td>Interventions</td></tr>
<tr><td>Evidence level:
4
Study type:
Retrospective Cohort Study
The purpose of this study was to analyze diagnostic and therapeutic modalities used in our medical center for the various tumor types and the different anatomical sites of occurrence.</td><td>Funding sources:
None

Conflict of Interests:
None

Randomization:

Blinding:

Dropout rates:</td><td>Total no. patients:
287 patients

Recruiting Phase:
1996 to 2015

Inclusion criteria:

Exclusion criteria:</td><td>Interventions:
Patients with benign tumors

Comparison:
Patients with malignant tumors</td></tr>
<tr><td>Notes:</td><td colspan="3">Oxford CEBM Level of Evidence 2011: EL 4 Retrospective Cohort Study

Retrospective study
No description of inclusion and exclusion criteria

Author's conclusion:</td></tr>
</table>

	Diagnostic and therapeutic modalities for treatment of salivary tumor at our hospital are presented and discussed with respect to others. A paradigm of therapy administered in our institute is presented.	
Outcome Measures/results	Primary Diagnostic and therapeutic modalities Secondary	Results: Of 287 cases, 216 had benign tumors and 71 had malignant tumors. Treatment was surgerybased in 99% of cases, often accompanied by radiotherapy and/or chemotherapy. Rates of imaging and biopsy for diagnosis were significantly higher in malignant than benign tumors. Fine-needle aspiration (FNA) was used in 90.3% of benign tumors. Of 71 malignant tumors, 69 underwent surgery to fully remove the malignant tumor. Adjuvant therapy included 22 neck dissections (30%), 28 radiotherapy (39.4%), 12 chemotherapy (16.9%) and 10 combined radio-chemotherapy (14.1%). Partial parotidectomy, submandibular sialoadenectomy and local excision were used in 78.1%, 8.3% and 6.9% of benign cases. Total parotidectomy, sub-total maxillectomy and wide excision were used in 16.9%, 12.7% and 22.6% of malignant cases

Papadogeorgakis, N. et al. Management of malignant parotid tumors. Oral Maxillofac Surg. 16. 29-34. 2012

Study type	Methodical Notes	Patient characteristics	Interventions
Evidence level: 4 Study type: Retrospective Cohort Study	Funding sources: None Conflict of Interests: None Randomization: Blinding:	Total no. patients: 31 Recruiting Phase: 1996 and 2008 Inclusion criteria: Patients with the diagnosis of primary malignant parotid tumors were admitted to our institution during the selected time frame Exclusion criteria:	Interventions: Management of patients with malignant parotid tumors Comparison:

	Dropout rates:	In six patients, surgery was not included in their treatment, due to advanced disease or poor medical condition, so they were excluded from this study	
Notes:	Oxford CEBM Level of Evidence 2011: EL 4 Retrospective Cohort Study Retrospective analysis of the patient-archive of a single center. No comparison group Author's conclusion: In conclusion, although the number of patients of this study is relatively small, we believe that the treatment of patients with malignant parotid tumors should be individualized according to the findings of each specific case. Regarding surgery, particular care and attention should be paid to maintaining all or part of the facial nerve whenever possible. We also believe that a preoperative diagnosis should be available for each patient, even when an open biopsy is necessary because it is of great importance if the surgeon knows the kind of tumor preoperatively, so he is able to plan surgery and inform the patient about it.		
Outcome Measures/results	Primary Oncologic efficacy of the treatment was evaluated, focusing on clinical outcome and especially survival. Secondary	Results: With reference to the extent of tissue removed, PSP was performed in 11 patients; SP, in 14 patients; and TRP, in 6 patients. The decision on the type of parotidectomy was determined by the ability to obtain a clear safety margin (at least 1 cm). In cases where the tumor extended to the deep lobe with intraoperative facial nerve invasion, a TRP was performed (6 cases; Table 2). In all cases of TRP and in four cases of SP (see below), the main trunk or branches of the facial nerve were sacrificed, and a reconstruction during surgery was attempted. For the reconstruction of the facial nerve, the great auricular nerve was used in four patients, ansa hypoglossus combined with great auricular in three patients, ansa hypoglossus in two patients, and in one patient, direct anastomosis was performed. In the 14 patients in which a typical SP was performed, the tumors were confined to the superficial lobe, but a clear margin could not be achieved without resecting the entire superficial lobe. In four of these patients, branches of the facial nerve were sacrificed. In the 11 patients who underwent a PSP, the tumor was confined to the superficial lobe, and a sufficient resection margin at the horizontal level could be achieved, while there was no presence of intraoperative facial	

		nerve invasion (Table 2). The median time of follow-up was 64 months, ranging from 8 to 144 months. Eight patients developed recurrences. Six patients died within the follow-up time. The overall survival rates at 5 and 10 years were 82.2% and 76.7%, respectively. The 5- and 10-year disease-free survival rates were 74.8% and 69.8%, respectively.

1.10 Sammlung 08. Wie effektiv ist eine elektive Neck Dissection in der Therapie maligner Speicheldrüsentumoren?

OXFORD (2011) Appraisal Sheet: Systematic Reviews

Luksic, I. et al. Elective neck dissection in adenoid cystic carcinoma of head and neck: yes or no? A systematic review. Eur Arch Otorhinolaryngol. 276. 2957-2962. 2019				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 3 Study type: Systematic Review of Retrospective Studies (18 studies, 5767 patients) Databases: PubMed, MEDLINE, EMBASE, Web of Science, ScienceDirect, and Scopus Search period: Inception to August 5, 2019 Inclusion Criteria: (1) AdCCHN, (2) primary surgical treatment including END, and (3) known data regarding occult neck disease rates. Exclusion Criteria: (1) specific diagnosis of adenoid cystic carcinoma could not be separated from other salivary gland tumours reported (aggregated salivary gland histology subtypes); (2) no information on lymph node status	Population: Patients with adenoid cystic carcinoma of head and neck (AdCCHN) Intervention: Elective neck dissection Comparison:	Primary: Occult neck metastases Secondary: Results: This analysis included a total of 5767 AdCCHN patients with 2450 ENDs, ranging from 10 to 1190. Elective lymphadenectomy was employed in 42.5% of patients with AdCCHN (range 9.2–100%). The overall rate of occult neck metastases in patients with AdCCHN was reported to range between 0 and 43.7%, the average being 13.9%. Author's Conclusion: If performed, END should be limited to levels I–III of the ipsilateral neck since occult metastases are exclusively located within these neck regions. Although END is associated with a prolonged regional recurrence-free period, it	18 studies (5767 patients) included: Agarwal 2008, Ali 2017, Amit 2013, Amit 2015, Balamucki 2012, Bhayani 2012, Cohen 2004, Cordesmeyer 2018, Garden 1995, Iyer 2010, Lee 2013, Lee 2014, Luksic 2016, Nobis 2014, Qian 2019, Stenner 2012, Wang 2012, Xiao 2019	

(clinically and histopathologic); (3) END rates not stated; (4) tumours that arose primarily at extremely rare subsites (lacrimal gland, external auditory canal) and those with low incidence (<0.5% overall) of occult neck disease (laryngeal AdCC); (5) less than ten cases of AdCCHN treated with END.		infuence on fnal outcome or survival is still controversial. This review strongly supports conduction of prospective trials on indications, prognostic signifcance and extent of END in AdCCHN.		
Methodical Notes				
Funding Sources: Not declared COI: Not declared Study Quality: Not investigated Heterogeneity: No meta-analysis was conducted Publication Bias: Not investigated Notes: Oxford CEBM Level of Evidence 2011: EL 3 Systematic Review of Retrospective Studies -No search for grey literature or unpublished studies was conducted -Insufficient description of search terms -Quality of the included primary studies was not investigated -No declaration of funding or conflict of interest				
Ning, C. et al. Cervical lymph node metastases in salivary gland adenoid cystic carcinoma: a systematic review and meta-analysis. Cancer Manag Res. 10. 1677-1685. 2018				

Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 3 Study type: Systematic Review and Meta-Analysis of Retrospective Studies (18 studies, 2993 patients) To determine whether neck dissection is necessary for the ACC of head and neck by analyzing the frequency of cervical lymph node metastases with meta-analysis. Databases: Web of Science, PubMed, and Ovid Search period: Inception to October 14, 2017 Inclusion Criteria: 1. Researches that investigated the frequency of cervical lymph node metastases in primary salivary gland ACC of head and neck. 2. The researches included data that can be extractable, and cervical lymph node metastases were confirmed by pathology. Exclusion Criteria: 1. Researches on patients who had	Population: Patients with primary salivary gland Adenoid cystic carcinoma (ACC) of head and neck Intervention: Comparison:	Primary: Frequency of cervical lymph node metastases Secondary: Results: In total, 18 studies involving 2993 patients were included in the analysis. Of the 2993 patients, 473 patients had cervical lymph node metastasis, with a merge frequency of 16% (95% CI: 13–19). Among included articles, only 4 involved cervical lymph node occult metastases, with a merge frequency of 14% (95% CI: 9–20). There were 5 articles containing minor salivary glands (MiSGs) involving 370 patients of which 92 patients had cervical lymph node metastases and the merge frequency was 25% (95% CI: 11–38). Moreover, there were 4 studies on major salivary glands involving 904 patients of which 158 patients had cervical lymph node metastases and the merge frequency was 17% (95% CI: 15–20). Author's Conclusion: Elective neck dissection is unnecessary for all patients with salivary gland ACC of head and neck. Moreover, compared with major salivary glands, MiSGs have a higher cervical lymph node metastases rate in ACC. The overall cervical lymph node metastases rate of MiSGs is 25%, which is enough to attract our attention. Therefore, we suggest that neck dissection might be applied to ACC of MiSGs.	18 studies (2993 patients): Bhayani 2012, Amit 2015, Min 2012, Liu 2015, Megwala and Sirjani 2017, Mücke 2010, van Weert 2013, Jang 2017, Ali 2017, Meyers 2016, Bjorndal 2015, Ko 2016, Hämetoja 2017, Mannelli 2017, Ouyang 2016, Zhang 2013, Kruse 2010, Lee 2014	

undergone preoperative radiotherapy and chemotherapy. 2. Researches that only investigated ACC of the upper respiratory or sinonasal. 3. Researches that only investigated clinical cervical metastases in salivary gland ACC. Single case reports and articles in languages other than English and Chinese were also excluded.				
Methodical Notes				
Funding Sources: Not described COI: None Study Quality: Unclear which tool was used for quality assessment. Among 18 included studies, 4 had a relatively low quality and 14 had a high-quality design as found by quality assessment. Heterogeneity: Chi-squared-based Q test and I 2 were used for heterogeneity evaluation. The fixed-effect model was used when there was no heterogeneity (P > 0.10 and I 2 < 0.10 or I2 >50%). Substantial heterogeneity was present for the outcomes: Overall cervical metastases rate (I2= 76%)and Metastases rate of ACC of MiSGs (I2=88%). Moderate heterogeneity for the outcome Cervical lymph node occult metastases rate (I2=56%) Publication Bias: Publication bias was evaluated using the Funnel plots. The relevant Funnel plot revealed that the majority of articles were close to axis and there was no publication bias in these researches for cervical lymph node overall metastases about ACC, cervical lymph node occult metastases, cervical lymph node metastases about ACC of MiSGs, cervical lymph node metastases rate about ACC of MaSGs Notes: Oxford CEBM Level of Evidence 2011: EL 3 Systematic Review and Meta-Analysis of Retrospective Studies				

-No search for grey literature or unpublished articles conducted -Inclusion criteria and PICO were not described sufficiently -Quality of the primary studies was investigated but not reported in detail in the review. Unclear which tool was used for the quality assessment -Substantial to moderate heterogeneity was present for the main outcomes which was not investigated or discussed	

NEWCASTLE - OTTAWA Checklist: Cohort

Harbison, R. A. et al. The role of elective neck dissection in high-grade parotid malignancy: A hospital-based cohort study. Laryngoscope. . . 2019			
Study type	Methodical Notes	Patient characteristics	Interventions
Evidence level: 4 Study type: Retrospective, multicenter cohort study To assess the effect of END on 3- and 5-year survival among cN0 patients with high-grade parotid cancer	Funding sources: This work was supported by a National Institute on Deafness and Other Communication Disorders grant (T32DC000018) Conflict of Interests: none Randomization: n.a. Blinding: n.a. Dropout rates: n.a.	Total no. patients: 1547 patients Recruiting Phase: January 1, 2004 and December 31, 2013 Inclusion criteria: Patients diagnosed as having parotid carcinomas from January 1, 2004 to December 31, 2013 were identified using the International Classification of Diseases for Oncology, Third Edition (ICD-O-3) topography code C07.9 Exclusion criteria: We excluded the following histologic subtypes: adenoid cystic carcinoma, skin cancers, other nonintrinsic tumors (e.g., Merkel cell, adnexal tumors, secretory carcinoma of breast, extra-adrenal paraganglioma, sarcomas, medulloblastoma, and granular cell tumors), hemangiopericytoma, and polymorphous low-grade adenocarcinoma. Given the distinct clinical behavior of adenoid cystic carcinoma (ACC) and that distant metastasis occurs in up to 40% of ACCs,17 we excluded ACC cases to minimize bias secondary	Interventions: Elective neck dissection (END) Comparison:

		to decreased survival from distant metastasis and differential clinical behavior from other histologies. Additionally, we excluded cases with ICD-O-3 morphological codes 8070, 8071, 8072, 8073, 8074, 8075, 8078, 8083, 8084, 8090, 8092, 8094, 8097, 8098, 8102, 8123, 8200, 8247, 8401, 8407, 8410, 8413, 8420, 8502, 8525, 8693, 8720, 8730, 8742, 8745, 8772, 9150, 9180, 9220, 9260, 9473, 9540, 9560, and 9580. In addition, patients with clinical evidence of nodal disease (cN1 or higher), patients with low-grade (grade 1 or 2) parotid malignancies, and cases diagnosed at the reporting facility that did not receive treatment at that facility. We also excluded cases where nodes were reported as examined by a pathologist without a corresponding neck dissection reported.	
Notes:	Oxford CEBM Level of Evidence: 4 Retrospective cohort study -Retrospective analysis of patient data -Multicenter experience Author's conclusion: This study did not find a statistically significant effect of END on survival at 3-years postdiagnosis after adjusting for potential confounders and treatment received. Therefore, we conclude that END may be used selectively in patients with clinically node-negative, high-grade parotid carcinoma given that they will likely achieve equivalent overall survival with adjuvant radiation. However, we cannot draw true causal inferences with the current data due to the lack of randomization. In summary, END is beneficial for prognostication and is therapeutic, especially in patients who are at risk of loss to follow-up or unable to receive adjuvant radiation, though prospective research is warranted to assess the effect of END on locoregional control among patients with cN0 high-grade parotid carcinoma.		
Outcome Measures/results	Primary 3- and 5-year survival Secondary	Results: This study did not find a statistically significant effect of END on survival at 3-years postdiagnosis after adjusting for potential confounders and treatment received. Therefore, we conclude that END may be used selectively in patients with clinically node-negative, high-grade parotid carcinoma given that they will likely achieve equivalent overall survival with adjuvant radiation. However, we cannot draw true causal inferences with the current	

		data due to the lack of randomization. In summary, END is beneficial for prognostication and is therapeutic, especially in patients who are at risk of loss to follow-up or unable to receive adjuvant radiation, though prospective research is warranted to assess the effect of END on locoregional control among patients with cN0 high-grade parotid carcinoma.

Kaura, A. et al. Utility of neck dissection for management of carcinoma of the parotid gland. Br J Oral Maxillofac Surg. . . 2019			
Study type	Methodical Notes	Patient characteristics	Interventions
Evidence level: 4 Study type: Retrospective Cohort Study To establish the frequency with which neck dissection was undertaken for parotid carcinoma within a London hospital, and to validate its use by establishing the incidence of metastasis to the cervical lymph nodes.	Funding sources: n.a. Conflict of Interests: None Randomization: n.a. Blinding: n.a. Dropout rates: n.a.	Total no. patients: 82 patients Recruiting Phase: 1992-2014 Inclusion criteria: Patients who had primary resection of parotid carcinomas at the head and neck unit between 1992 and 2014. Exclusion criteria: One patient was excluded as it was not possible to establish the T stage.	Interventions: Neck dissection in the treatment of carcinoma of the parotid gland Comparison:
Notes:	Oxford CEBM Level of Evidence 2011: EL 4 Retrospective Cohort Study -Retrospective analysis of patient data -Single-center experience Author's conclusion:		

	The findings of this study support the use of routine neck dissection for the treatment of high-grade, invasive carcinoma ex-pleomorphic adenoma, salivary duct carcinoma, high-grade adenocarcinoma NOS, adenoid cystic carcinoma, and high-grade acinic cell carcinoma	
Outcome Measures/results	Primary Incidence of metastatic disease Secondary	Results: The group comprised 82 patients (42 women and 40 men, median (range) age 57 (10 – 84) years). A total of 54 of the 82 patients identified had neck dissections. Forty-three of the 54 who had neck dissections had had a preoperative diagnosis of carcinoma, and seven had had a preoperative diagnosis that was suspicious of malignancy. Nodal metastases were detected in 10 with high-grade, invasive carcinoma ex-pleomorphic adenomas, two with salivary duct carcinomas, one with a high-grade adenocarcinoma not otherwise specified (NOS), one with an adenoid cystic carcinoma, and one with a high-grade acinic cell carcinoma. No metastases were found in those with a low-grade acinic cell carcinoma, low-grade mucoepidermoid carcinoma, epithelial-myoepithelial carcinoma, or non-invasive carcinoma ex-pleomorphic adenoma. Median survival was 2.11 years and five-year survival between 11% and 22%. Ten-year estimated survival was between 0 and 11%.

1.11 Sammlung 09. Wie effektiv ist die lokale Re-Operation zur Herstellung des Sicherheitsabstandes bei erst nachträglich histologisch gesicherten malignen Tumoren der Glandula parotis?

NEWCASTLE - OTTAWA Checklist: Cohort

Zhang, X. et al. Reoperation following the use of non-standardized procedures for malignant parotid tumors. Oncology Letters. 14. 6701-6707. 2017			
Study type	Methodical Notes	Patient characteristics	Interventions
Evidence level: 3 Study type: Cohort Study	Funding sources: None Conflict of Interests: None Randomization: n.a. Blinding: n.a. Dropout rates: n.a.	Total no. patients: 30 Recruiting Phase: January 2008 and December 2014 Inclusion criteria: i) The patient had a malignant parotid tumor and was recommended by their primary surgeon for transfer to a higher tier hospital for reoperation; ii) the patient underwent a primary surgery comprising partial tumor resection, tumor enucleation and partial superficial lobe parotidectomy; iii) the patient underwent physical examination and enhanced computed tomography (CT) scans that revealed residual tumor, or prompted suspicion of residual tumor, at the primary tumor site or showed cervical lymph node enlargement; iv) the patient was aged between 18 and 70 years; v) the patient had a Karnofsky performance score of >80 (10);	Interventions: Reoperation procedures Reoperation of malignant parotid tumors. Total parotidectomy was performed on all patients for management of the primary tumor. Selective or functional neck dissection was performed in patients with undifferentiated carcinoma, poorly differentiated mucoepidermoid carcinoma, squamous cell carcinoma, adenocarcinoma or cystadenocarcinoma at cN0 stage. For patients identified to have cervical lymph node enlargement preoperatively by physical examination or enhanced CT scan, a functional or radical neck dissection of the level I-IV nodes was performed according to lymph node status, as described above. For patients with tumor invasion of the skin in the parotid region, flap repair surgery was performed according to the individual skin defect conditions. Facial nerve procedures En bloc resection of the tumor with the facial nerve

		vi) the expected survival time of the patient was >1 year; and vii) the patient voluntarily signed informed consent forms. Exclusion criteria: i) >3 months had elapsed since the primary surgery; ii) the patient had any other malignant tumors of the head and neck; iii) the patient had a history of head and neck radiotherapy; and iv) the patient had severe heart, lung, liver or kidney disease.	was performed if facial paralysis was present prior to surgery. If the tumor was attached to the nerve, the nerve was preserved if separation was possible, postoperative adjuvant radiotherapy (60 Gy in 30 fractions for 6 weeks) was administered. The facial nerve was excised in the event that separation from the tumor mass was difficult, or if the facial nerve was confirmed to pass through the tumor. Following partial or complete excision of the facial nerve, facial nerve reconstruction was performed if possible. The House Brackmann facial nerve grading system was used to assess facial nerve function following its reconstruction Radiation therapy All patients who underwent reoperation required supplementary postoperative radiation therapy Comparison: No comparison group
Notes:	Oxford CEBM Level of Evidence 2011: EL 3 Cohort Study -Single center study -No control group -No blinding of the outcome assessors was performed -Number of included patients was small		

	Author's conclusion: The current findings indicate that the qualitative diagnosis of malignant parotid tumors prior to surgery is difficult, there is a high incidence of residual tumor following non-standardized procedures, and that reoperation in a timely manner is required in such cases.	
Outcome Measures/results	Primary Primary tumor, facial nerve involvement, complications, overall survival Secondary	Results: A total of 30 patients who met the inclusion criteria, were diagnosed with a malignant parotid tumor and underwent reoperation following the use of a non-standardized procedure were included in the present study. Surgical conditions and clinical data were analyzed. Among the patients with a malignant parotid tumor who underwent reoperation subsequent to a non-standardized procedure, the incidence of residual tumor, as confirmed by pathological examination, was 63.3% (19/30). Morbidity The intact facial nerve preservation rate was 83.3% (25/30), the facial nerve branch resection rate was 6.7% (2/30), the facial partial nerve resection rate was 6.7% (2/30) and the facial nerve resection rate was 3.3% (1/30). In total, 3 patients underwent facial nerve reconstruction, 3 patients underwent a local flap repair of skin defects in the parotid region and 3 patients underwent pectoralis major muscle flap repair. Mortality and Recurrence A total of 3 patients experienced local recurrence and 5 mortalities were reported, of which 2 patients with adenoid cystic carcinoma succumbed to lung metastasis, 1 patient with atypical poorly differentiated adenocarcinoma succumbed to brain metastases, and 2 patients with poorly differentiated mucoepidermoid carcinoma succumbed to local recurrence. As analyzed using Kaplan-Meier estimator curves, the 5-year local control rate was 87.2%, the 5-year recurrence-free survival rate was 88.1% (Fig. 2) and the 5-year overall survival rate was 81.7%.

1.12 Sammlung 11. Welche Optionen stehen für die Therapie eines Lokalrezidivs (maligner) Speicheldrüsentumore nach primär chirurgischer Therapie zur Verfügung?

OXFORD (2011) Appraisal Sheet: Systematic Reviews

Mc Loughlin, L. et al. The role of adjuvant radiotherapy in management of recurrent pleomorphic adenoma of the parotid gland: a systematic review. European Archives of Oto-Rhino-Laryngology. 276. 283-295. 2019				
Evidence level/Study Types	P - I - C	Outcomes/Results	Literature References	
Evidence level: 3 Study type: Systematic Review of retrospective cohort studies (8 studies, 366 patients) The aim of this study was to determine whether adjuvant radiotherapy is more effective than surgical resection alone in patients with recurrent pleomorphic adenoma of the parotid gland, in terms of further recurrence, malignant transformation and treatment-related complications. Databases: Pubmed, OVID, EBSCO, Embase, The Cochrane Library, SCOPUS and OpenGrey databases Search period: 1988 to 2018 Inclusion Criteria: 1. The study was a randomized controlled trial, non-	Population: Patients with recurrent pleomorphic adenoma of the parotid gland Intervention: Adjuvant radiotherapy Comparison: Surgical resection alone	Primary: Further disease recurrence following treatment Secondary: Secondary outcomes included malignant transformation to carcinoma ex-pleomorphic adenoma, and treatment complications—facial weakness and secondary radiationinduced malignancy Results: Of 891 records screened, eight studies were included, assessing 366 participants. Two noted a benefit of adjuvant radiotherapy in reducing further recurrence. The remainder did not show significant benefit, although four showed a trend towards lower rates. Only one case of malignant transformation was identified in a patient not irradiated. Similar rates of facial nerve dysfunction were identified between groups. Author's Conclusion: The available evidence	8 studies (366 patients) included: Malard 2013, Abu-Ghanem 2016, Renehan 1996, Carew 1999, Liu 1995, Radaelli de Zinis 2008, Makeieff 2010, Yugeros 1998	

randomized controlled trial, prospective or retrospective cohort study. 2. The study reported on outcomes in patients treated for recurrent pleomorphic adenoma of the parotid gland. 3. The study compared benefits and adverse effects of surgery alone and surgery combined with adjuvant radiotherapy. Exclusion Criteria: 1. It reported on outcomes in patients treated with primary rather than adjuvant radiotherapy. 2. It had no comparison group. 3. It was a case report or abstract with insufficient data for inclusion. 4. There was no English translation available.		suggests that adjuvant radiotherapy reduces recurrence rates in patients with recurrent pleomorphic adenoma and certain adverse prognostic factors. While it appears not to have significant adverse effects, given the lack of prospective evidence, we recommend careful use in patients at high risk of further recurrence and further research in the form of well-designed randomised controlled trials.		
Methodical Notes				
Funding Sources: Not described COI: None Study Quality: The Newcastle-Ottawa Scale for Cohort Studies was used to assess quality of the included studies. Quality analysis scores using the Newcastle-Ottawa Scale for Cohort Studies ranged from 3 to 7 points, with six studies scoring 5 points from a maximum of 9. None were excluded due to poor quality. Heterogeneity: No meta-analysis was conducted				

Publication Bias: Less than ten trials were included, therefore an investigation of publication bias was not possible Notes: Oxford CEBM Level of Evidence 2011: EL 3 Systematic Review of retrospective cohort studies -No search for unpublished articles or inspection of reference lists was conducted -The number of included patients was small (366)	

OXFORD (2011) Appraisal Sheet: Prognostic Studies

Grzybowska-Szatkowska, L. et al. The retrospective analysis of recurrent salivary gland cancer after surgery and adjuvant radio- or chemoradiotherapy. Nowotwory. 68. 245-252. 2018			
Population	Intervention	Outcomes/Results	
Evidence level: 4 Study type: Retrospective Study To analyse the survival and progression rates in patients with recurrent salivary gland cancer after surgery and adjuvant radio- or chemotherapy Number of Patient: 43 Recruitung Phase: 2006-2016 Inclusion Criteria: Patients treated for cancer of the large salivary glands in the Centre of Oncology of the Lubelskie Region, Poland, in the years 2006–2016. Patients underwent radical surgery, followed by radical radio or chemoradiotherapy. A retrospective analysis of the disease history allowed the identification of 43 patients with a recurrent disease. Exclusion Criteria: n.a.	Intervention: / Comparison: /	Primary: Progression-free survival (PFS) and overall survival (OS). Secondary: Results: Of all 43 relapses, 28 (65%) were locoregional. There were 22 relapses in the surgical bed (these were recurrences in the primary tumour area, in the area of removed salivary glands and in the area of primarily involved lymph nodes). In 6 patients, recurrences were observed in the regional lymph nodes beyond the surgical bed. Only one of these recurrences was found beyond the irradiated area. Of 11 systemic relapses, 7 occurred in the lungs, 3 in the liver, 2 in the bones, 2 in the brain and 1 in the mediastinal lymph nodes The 6-, 12- and 24-month OS rates were: 51%, 41%, and 14%, respectively, while the 6-, 12- and 24-month PFS rates were: 44%, 27%, and 14%, respectively. Any treatment improves OS and PFS, with surgery having the greatest effect on improving PFS, followed by chemotherapy and radiotherapy. A multivariate analysis has shown that predictors of PFS are: irradiated volume and radiation technique, while irradiated volume is the predictor of OS. Author's Conclusion: Prognosis in patients with recurrent gland	

		cancer is poor and does not depend on the type of relapse, but rather on further management.	
Methodical Notes			
Funding Sources: n.a. COI: None. Randomization: n.a. Blinding: n.a. Dropout Rate/ITT-Analysis: n.a. Notes: Oxford CEBM Level of Evidence 2011: EL 4 Retrospective Study			
Li, B. B. et al. A case-cohort study of recurrent salivary adenoid cystic carcinoma after iodine 125 brachytherapy and resection treatment. Annals of Diagnostic Pathology. 19. 1-5. 2015			
Population	Intervention	Outcomes/Results	
Evidence level: 4 Study type: Retrospective Chart Review Number of Patient: 140 patients Recruitung Phase: 2001-2012 Inclusion Criteria: AdCCs originating from the salivary glands, (ii) gross tumor resection	Intervention: Primary surgery followed by 125I radioactive seed implantation. Comparison:	Primary: The investigated parameters included the sex and age distributions, anatomic location, TNM stage, histologic type, tumor characteristics, treatment before seed implantation, surgical findings, and postoperative outcomes. Secondary: Results: 140 Patients of adenoid cystic carcinoma (AdCC), who underwent resection and iodine 125 (125I) radioactive seed implantation, were recruited for this study	

performed before seed implantation, and (iii) primary and recurrent tumor mass diagnosed by 2 professional pathologists. Exclusion Criteria:		Among these 140 patients, 16 patients (9 women and 7 men) aged between 34 and 72 years (median age, 49.5 years) had recurrent tumors. The primary locations were palate (6 cases), parotid (5 cases), sublingual gland (2 cases), submandibular gland (1 case), tongue (1 case), and buccal gland (1 case). All patients were followed up averagely for 61 months (from 12 to 96 months). No serious radiotherapeutic side effect was observed among all the cases The 3-year local control rate of rAdCC was 51.6%, and the overall disease-specific survival rate was 49.4%. Eight patients showed distant metastasis (50%, 8/16) (6 cases of lung metastases and 2 cases of lymph node metastases in the neck). The histologic grades of 10 rAdCCs were upgraded (62.5%, 10/16). Two cases displayed sarcomatous transformation after brachytherapy (1.4%, 2/140). Six patients died of lung metastasis, and 1 patient was lost to follow-up. At the time of analysis, the 3-year overall disease-specific survival was 49.4% Author's Conclusion: Although the overall local control rate and survival rate were relatively favorable, some rAdCCs with an aggressive phenotype appeared to respond poorly to 125I seed implantation. Preventive adjuvant chemotherapy should be prescribed for these rAdCCs	
Methodical Notes			
Funding Sources: None COI: None Randomization: n.a.			

Blinding: n.a. Dropout Rate/ITT-Analysis: n.a. Notes: Oxford CEBM Level of Evidence 2011: EL 4 Retrospective chart review -Retrospective analysis of patient data -Single center experience	

NEWCASTLE - OTTAWA Checklist: Cohort

Gidley, P. W. et al. The results of temporal bone surgery for advanced or recurrent tumors of the parotid gland. Laryngoscope. 121. 1702-7. 2011			
Study type	Methodical Notes	Patient characteristics	Interventions
Evidence level: 4 Study type: Retrospective Review To describe the results of temporal bone surgery in managing advanced or recurrent tumors of the parotid gland.	Funding sources: None Conflict of Interests: None Randomization: n.a. Blinding: n.a. Dropout rates: n.a.	Total no. patients: 49 patients Recruiting Phase: 2002 to July 2009 Inclusion criteria: Patients who required either mastoidectomy or temporal bone resection for malignancies involving the parotid gland from January 2002 to July 2009 Exclusion criteria:	Interventions: Mastoidectomy or temporal bone resection Comparison:
Notes:	Oxford CEBM Level of Evidence 2011: EL 4 Retrospective Cohort Study -Retrospective analysis of patient data -Single center experience Author's conclusion: Mastoidectomy and temporal bone resection permit preservation of the facial nerve when oncologically safe; they may help to achieve negative margins, and they allow facial nerve grafting when nerve sacrifice is required. Despite the poor prognostic indicators of facial paralysis, recurrent tumors, and perineural invasion, a significant number of patients can be salvaged successfully when a temporal bone procedure is combined with parotidectomy		

Outcome Measures/results	Primary Recurrence and survival rates Secondary	Results: Forty-nine patients were identified who required either mastoidectomy (n = 33) or temporal bone resection (n = 16) for malignancies involving the parotid gland. Facial nerve sacrifice was required in 35 patients (71.4%). Perineural invasion was found in 51.1% of patients; and negative margins were achieved in 78.2% patients. Six of 10 patients presenting with normal facial function (House-Brackmann I) and recurrent tumors maintained normal facial function following salvage surgery. Trismus, tumors larger than 4 cm, and the need for mandibulectomy were significantly correlated with higher recurrence rates (P = .025, P = .004, and P = .002, respectively). Patients with preoperative House-Brackmann I or II had a lower risk for recurrence (P = .035) and more favorable survival at 3 years (P = .024). Patients who required parapharyngeal space dissection and those with metastatic neck disease had the poorest survival rates. The overall survival at 3 years was 72.4%.

Karam, S. D. et al. Reirradiation of recurrent salivary gland malignancies with fractionated stereotactic body radiation therapy. J Radiat Oncol. 1. 147-153. 2012

Study type	Methodical Notes	Patient characteristics	Interventions
Evidence level: 4 Study type: Retrospective cohort study To review a single institution experience with the reirradiation of recurrent salivary gland tumors using fractionated stereotactic radiosurgery (SBRT).	Funding sources: n.a. Conflict of Interests: none Randomization: n.a. Blinding: n.a.	Total no. patients: 18 patients Recruiting Phase: 2003 and 2011 Inclusion criteria: Eligible patients were diagnosed with recurrent malignant salivary gland tumors and were treated with definitive SBRT reirradiation either as a primary or adjuvant modality at the Georgetown University Hospital between September 2003 and March 2011. All patients had histologically proven	Interventions: Reirradiation of recurrent salivary gland tumors using fractionated stereotactic radiosurgery (SBRT) Comparison:

	Dropout rates: n.a.	disease. Details of the previous radiation therapy were available for all patients with prior history of salivary gland irradiation. Exclusion criteria:	
Notes:	Oxford CEBM Level of Evidence 2011: EL 4 Retrospective cohort Study -Retrospective analysis of patient data -Single center experience -Small number of included patients Author's conclusion: This study has demonstrated the feasibility of using fractionated SBRT reirradiation of recurrent tumors with response rates comparable to other treatment modalities. At early follow-up, treatment was generally well tolerated, but caution needs to be exercised with higher doses to prevent STN. Our retrospective review is, however, limited by potential selection bias, sample size, and heterogeneous patient population and treatment parameters. Future studies with larger sample size, longer follow-up, and less histological variability are warranted.		
Outcome Measures/results	Primary Overall survival (OS), progression-free survival (PFS), and local control (LRC) Secondary	Results: Patient characteristics 18 patients diagnosed with recurrent, previously irradiated, salivary gland carcinomas were treated with SBRT reirradiation. Median age was 68 for all patients with most tumors being of major salivary gland origin. Most patients did not undergo surgical resection, and among those that did, all had positive margins. Only seven patients received chemotherapy, and the median SBRT dose was 30 Gy given in five fractions with a median cumulative dose of 91.1 Gy. Results The median overall survival (OS), progression-free survival (PFS), and local control (LRC) were 11.5, 3.5, and 5.5 months, respectively. The 2-year OS, PFS, and LRC rates were 39%, 24%, and 53%, respectively. Statistical analysis identified presence of gross disease and interval to reirradiation as negative predictors of survival outcomes on both univariate and multivariate	

		analyses ($p < 0.05$). On multivariate analysis, tumor volume was a negative predictor of survival outcomes ($p < 0.05$). Long-term toxicity analysis revealed four patients in the reirradiated group with soft tissue necrosis, which correlated with the cumulative dose ($p = 0.01$).

1.13 Sammlung 12. Welche Optionen stehen für die Therapie eines Lokalrezidivs (maligner) Speicheldrüsentumore nach primär nicht-chirurgischer Therapie zur Verfügung?

NEWCASTLE - OTTAWA Checklist: Cohort

Wald, P. et al. Intraoperative electron beam radiotherapy for locoregionally persistent or recurrent head and neck cancer. Head and Neck. 41. 2148-2153. 2019			
Study type	Methodical Notes	Patient characteristics	Interventions
Evidence level: 4 Study type: Retrospective Cohort Study To report our institutional experience with intraoperative radiotherapy for persistent or recurrent head and neck cancer.	Funding sources: n.a. Conflict of Interests: None. Randomization: n.a. Blinding: n.a. Dropout rates: n.a.	Total no. patients: 61 patients Recruiting Phase: 2006 and 2014 Inclusion criteria: Patients who underwent gross total resection and IORT for persistent or recurrent head and neck cancer between 2006 and 2014 at The Wexner Medical Center at The Ohio State University. Patients were allowed, but not required, to have received postoperative radiation and/or systemic therapy Exclusion criteria:	Interventions: Intraoperative radiation therapy (IORT). After maximal salvage surgery, IORT was delivered using a mobile electron unit. A single fraction was delivered to a median dose of 12.5 Gy (range, 10-17.5 Gy). In general, doses of 10-12.5 Gy were used for gross total resection, while higher doses of 15-17.5 Gy were used in cases of gross residual disease or surgeon concern regarding microscopic margin status. Dose was prescribed to the 90% isodose line in all but two patients (prescribed to 100% isodose line), and 6 MeV electrons were used for all but five patients. Comparison:
Notes:	Oxford CEBM Level of Evidence 2011: EL 4 Retrospective Cohort Study -Retrospective analysis of patient data -Single institution experience		

	-No control group Author's conclusion: IORT has shown effective LRC and OS with an acceptably low rate of severe toxicity at our institution. OS was significantly better for non-SCC histology. For SCC patients, there is a trend toward improved PFS and OS associated with negative surgical margins.	
Outcome Measures/results	Primary Disease recurrence and overall survival Secondary	Results: Patient characteristics: 39 men and 22 women with a median age of 58 years (range, 26-86). Fifty-five (90%) patients were treated for recurrent disease and 6 (10%) patients were treated for persistent disease after nonsurgical treatment. Forty-one (67%) patients were treated for disease at the primary site and 20 (33%) patients were treated for regional neck disease. The most common primary disease sites were oropharynx, oral cavity, and sinonasal cavities. Forty-five (74%) patients had squamous cell carcinoma. Twenty-eight (46%) patients had positive final surgical margins documented. Median follow-up among 17 surviving patients was 15.9 months (range, 4.9-74.4 months). Results: Overall survival (OS) Median overall survival (OS) was 19.1 months, respectively. The 1-, 2-, and 3-year rates of OS were 62%, 42%, and 34%, respectively. OS was significantly better for non-SCC patients (median 37.7 vs 15.0 months, P = .03). For the SCC only group, median OS was 15 months. The 1-, 2-, and 3-year rates of OS were 60%, 32%, and 17%, respectively (Figure 2). There was a trend toward improved OS associated with negative surgical margin (median 16.1 vs 9.6 months, P = .06). There were no significant differences in OS based on adjuvant therapies received Disease-free survival Median disease-free survival (PFS) was 9.8 months, respectively. The 1-, 2-, and 3-year rates of DFS were 39%, 19%, and 11%, respectively. There was a trend toward improved DFS associated with non-SCC histology (median 18.1 vs 8.3 months, P = .09). For the SCC only group, median DFS was 8.3 months. The 1-, 2-, and 3-year rates of DFS were 28%, 15%, and 9%, respectively. There was a trend toward improved DFS associated with negative surgical margin (median 7.4 vs 4.5 months, P = .09). There were no significant differences in DFS based on adjuvant therapies received.

		Locoregional control (LRC) One-, 2- and 3-year rates of locoregional control were 59%, 35%, and 27% respectively. For the SCC only group (n = 45), median time to locoregional failure was 14.5 months. The 1-, 2-, and 3-year rates of LRC were 55%, 30%, and 18%, respectively. There were no statistically significant differences in LRC based on histology (SCC vs non-SCC), surgical margins, adjuvant EBRT, or adjuvant chemotherapy Distant control There were 25 (25/61, 41%) patients who developed distant metastases during follow-up. Twenty-two (22/61, 36%) developed distant metastases as their first site of recurrence. Of these patients, 13 developed synchronous locoregional recurrence (13/22, 59%) and nine of them had an interval of distant-only recurrence (9/22, 41%). The most common sites of distant progression were lung, bone, and brain.

1.14 Sammlung 13. Wie sollte eine effektive Nachsorge für ehemalige Speicheldrüsenpatienten gestaltet sein?

OXFORD (2011) Appraisal Sheet: Diagnostic Studies

Lee, S. H. et al. Detection of distant metastasis and prognostic prediction of recurrent salivary gland carcinomas using (18) F-FDG PET/CT. Oral Dis. 24. 940-947. 2018				
Evidence level/Study Types	Population	Outcomes/Results		
Evidence level: 3 Study type: Retrospective Diagnostic Study To compare the diagnostic accuracy of 18F-FDG PET/CT and conventional contrast-enhanced CT for the re-staging of recurrent salivary gland carcinoma (SGC).	Number of patients / samples: 58 patients Reference standard: Histological examinations or follow-up/confirmation imaging Validation: The sensitivity, specificity, accuracy, positive-predictive values (PPV), and negative-predictive values (NPV) of 18F-FDG PET/CT and ceCT images were calculated with 95% confidence intervals (CIs). MCNemar's test was used to compare the sensitivity, specificity, and accuracy of 18F-FDG PET/ CT vs ceCT. Receiver operating characteristic (ROC) curves were generated to compare the 18F-FDG PET/CT results with those of the ceCT. Blinding: Assessors were blinded	Results: Of 58 patients with recurrent SGCs, 17 (29%) had a local recurrence, 17 (29%) had a regional recurrence, and 38 (66%) had a distant metastasis, with these classifications showing overlap. During the median follow-up of 68 months (12–256 months), 25 (43%) patients died due to disease progression; at their last followup, 13 (22%) patients were alive with no evidence of recurrent disease, and 19 (33%) were alive with disease. The 5-year PFS and OS of all study participants were 39,8% and 51.1% respectively. The sensitivity and accuracy of 18F-FDG PET/CT for the detection of distant metastases were significantly higher than those of CT ($p < 0.05$), whereas, for detection of loco-regional recurrences, they did not differ ($p > 0.1$). The 18F-FDG PET/CT-positive findings at distant sites were predictors of poor progression-free and overall survival outcome (all $p < 0.05$).		

	Inclusion of clinical information: Dealing with ambiguous clinical findings:	Author conclusions: 18F-FDG PET/CT is a more effective method than CT for detecting distant site recurrences of SGC. This may lead to prognostic prediction for recurrent SGCs.		
Methodical Notes				
Funding Sources: n.a. COI: None. Notes: Oxford CEBM Level of Evidence 2011: EL 3 Retrospective diagnostic study with reference standard and blinding				
Razfar, A. et al. Positron emission tomography-computed tomography adds to the management of salivary gland malignancies. Laryngoscope. 120. 734-8. 2010				
Evidence level/Study Types	Population	Outcomes/Results		
Evidence level: 4 Study type: Retrospective Chart Review To evaluate the efficacy of combined positron emission tomography-computed tomography (PET-CT) in identifying salivary gland malignancies and to examine the role of PETCT in the management of these patients	Number of patients / samples: 55 patients Reference standard: n.a. Validation: We determined sensitivity, specificity, negative predictive value, and positive predictive value of PET-CT in predicting the presence of malignancy Blinding: n.a.	Results: Overall, PET-CT demonstrated a sensitivity of 74.4%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 61.5%. PET-CT also identified unrecognized distant metastases in the following sites: six lung, five bone, two distant lymph nodes, and one liver. PET-CT added to management in 26 patients (47.3%), and it was the deciding diagnostic modality in eight patients (14.5%). Of these 26 patients, 14 patients underwent additional surgery. Three patients with recurrence underwent PET-CT scan-directed radiation and/or chemotherapy, whereas nine patients diagnosed with distant disease received palliative treatment. Author conclusions: PET-CT is effective in the evaluation of salivary cancers and is particularly useful in initial staging and		

	Inclusion of clinical information: Dealing with ambiguous clinical findings:	for surgical and radiation therapy planning. Although the combined PET-CT is a valuable adjuvant, there appears to be less added benefit in long-term surveillance and detecting distant metastasis where CT alone with contrast is likely sufficient for this group of patients. Added information from PET-CT can help guide management, especially when determining whether a patient is a candidate for definitive or palliative treatment.		
Methodical Notes				
Funding Sources: None. COI: None. Notes: Oxford CEBM Level of Evidence 2011: EL 4 Retrospective Chart Review without reference standard or blinding				

1.15 Sammlung 14. Besitzt bei malignen Tumoren der Gl. Parotis die Resektion des N. facialis einen Überlebensvorteil gegenüber dem Nerverhalt und anschließender Radiotherapie?

OXFORD (2011) Appraisal Sheet: Prognostic Studies

Gomez, D. R. et al. Clinical and pathologic prognostic features in acinic cell carcinoma of the parotid gland. Cancer. 115. 2128-37. 2009			
Population	Intervention	Outcomes/Results	
Evidence level: 3 Study type: Retrospective prognostic cohort study. "To determine patterns of failure	Intervention: Exposure to risk factors	Primary: DFS, OS, LC, and DMFS Secondary: local, regional, distant failure, treatment toxicity Results: Study population: The T classifications were as follows: T1 in 46% of	

and adverse prognostic features." Number of Patient: 38 consecutive patients. Recruitung Phase: From March of 1989 to August of 2006, Inclusion Criteria: Patients with Acinic Cell Carcinoma (AciCC) of the parotid gland undergoing surgery. Exclusion Criteria: -	Comparison: Non-exposure	patients, T2 in 23% of patients, T3 in 18% of patients, and T4 in 9% of patients. Three patients had cervical lymph node involvement. All patients underwent surgery as their primary treatment. Approximately 63% of patients (n = 22) received radiation treatment. The median follow-up time for surviving patients was 59.9 months. Results: Five-year estimates of disease-free survival (DFS), overall survival (OS), and local controlwere 85%, 90%, and 90%, respectively.Of the clinical variables tested, clinical extracapsular extension (ECE), facial nerve sacrifice, and lymph node involvement were found to be significantly associated with a detriment in DFS and OS (P < .05). Positive surgical margins, histologic ECE, >2 mitoses per 10 high-power fields (HPF), atypical mitosis, vascular invasion, perineural invasion, pleomorphism, and necrosis were associated with adverse DFS (P < .05). All of these variables except for vascular invasion (P < .377) and perineural invasion (P<.07 associated with os. if high-grade tumorswere defined on the basis of high mitotic activity>2 mitoses/10 HPF) and/or tumor necrosis, high-grade carcinomas had a significantly lower DFS and OS (P <.001> Author's Conclusion: AciCC had a low treatment failure rate, and a large number of patients could be considered candidates for surgery only. A histologic grading system was devised to help stratify patients for adjuvant treatment.	
Methodical Notes			
Funding Sources: The authors made no disclosures. COI: The authors made no disclosures. Randomization: not applicable Blinding: Blinding was not performed. Dropout Rate/ITT-Analysis: -			

Notes: Oxford level of evidence: 3 retrospectieve prognostic cohort study.			
Guntinas-Lichius, O. et al. Primary Parotid Malignoma Surgery in Patients with Normal Preoperative Facial Nerve Function: Outcome and Long-Term Postoperative Facial Nerve Function. Laryngoscope. 114. 949-956. 2004			
Population	Intervention	Outcomes/Results	
Evidence level: 3 Study type: Retrospective cohort study. Number of Patient: 107 Recruitung Phase: Medical records of 211 patients treated from 1986 to 2000 in an university hospital of Cologne (Cologne, Germany) were reviewed. Inclusion Criteria: Patients with patients with newly diagnosed parotid gland cancer who were primarily treated with surgery and had normal facial nerve function. Exclusion Criteria: Patients with recurrent disease or metastasis within the parotid gland attributable to other primary tumor origin and patients with malignant lymphoma were not included.	Intervention: facial nerve preservation. Comparison: non-preservation.	Primary: Facial nerve outcome (electromyography), oncological outcomes. Secondary: - Results: 91 patients had a normal preoperative function. Facial nerve preservation during surgery by total parotidectomy was possible in 79 patients, whereas in 28 patients a radical parotidectomy was necessary. Otherwise, the oncological characteristics of both groups were not different. Directly after total parotidectomy, half of the patients presented a facial paresis but only two patients (2%) developed a permanent partial paresis. The 5-year disease-free rate and the 5- and 10- year survival rates were 65%, 83%, and 54%, respectively. After radical parotidectomy, the results were not significantly different. The 5-year disease-free rate and the overall 5- and the 10-year survival rates were 56%, 62%, and 42%, respectively. Author's Conclusion: "Treatment of primary parotid cancer with preoperatively normal facial nerve function by standardized parotidectomy and precise microsurgical preservation preservation of the facial nerve is often possible. This approach demonstrates favorable oncological results with a low level of long-term facial nerve morbidity."	
Methodical Notes			

Funding Sources: - COI: - Randomization: - Blinding: - Dropout Rate/ITT-Analysis: - Notes: Oxford level of evidence: 3 retrospective cohort study.	

Iseli, T. A. et al. Facial nerve sacrifice and radiotherapy in parotid adenoid cystic carcinoma. Laryngoscope. 118. 1781-1786. 2008

Population	Intervention	Outcomes/Results
Evidence level: 2 Study type: Retrospective inception cohort study. "To evaluate the impact of facial nerve sacrifice and postoperative radiotherapy on the outcome of adenoid cystic carcinoma of the parotid gland." Number of Patient: 52. Recruitung Phase: Patients files were accessed from University of Iowa database and were inpatients betweeen 1966 and August, 2007.	Intervention: Facial nerve preservation / sacrific. Comparison: Facial nerve sacrifice.	Primary: Quantitative assessments of recurrence and survival and qualitative assessments of health-related quality of life. Secondary: - Results: 52 (follow-up mean: 9.1 years, range: 0.5–40.8 years) demonstrated local control rates of 84.6% (5 years), 76.9% (10 years), and 50% (20 years). Compared with facial nerve preservation, facial nerve sacrifice had better control at 5 years (100 vs. 78.9% P = .259) while having detrimental effects on eating, speech, and esthetics. Local control at 5 years was significantly better (P = .048) with postoperative radiotherapy (100%) than without (84.6%). Overall survival was 79.4% (5 years), 50% (10 years), and 32.3% (20 years). At 10 years, there was a trend toward improved survival with facial nerve sacrifice (58.8 vs. 46.8%, P = .569) and postoperative radiotherapy (62.4 vs. 39.3%, P = .409). 11 patients with lung metastases survived an average of 67.8 months after

Inclusion Criteria: Patients with parotid adenoid cystic carcinoma. Exclusion Criteria: -		metastases were identified. Only 4 of 46 patients N0 patients (8.3%) subsequently developed lymph node metastases. Author's Conclusion: Selective facial nerve sacrifice was associated with trends toward improved local control and survival but worse quality of life. Patients managed with postoperative radiotherapy had better local control rates than those without. N0 patients rarely developed metastases to regional lymph nodes.	
Methodical Notes			
Funding Sources: not declared. COI: not declared. Randomization: - Blinding: - Dropout Rate/ITT-Analysis: - Notes: Oxford level of evidence: 2 inception cohort study Unclear description of inclusion criteria. No declaration of potential conflicts of interest.			

Otsuka, K. et al. Clinical Outcomes and Prognostic Factors for Salivary Duct Carcinoma: A Multi-Institutional Analysis of 141 Patients. Ann Surg Oncol. 23. 2038-45. 2016

Population	Intervention	Outcomes/Results	
Evidence level: 4 Study type: Retrospective, prognostic,	Intervention: - partial parotidectomy and total parotidectomy,	Primary: Overall survival (OS) and disease-free survival (DFS) Secondary: Treatment failure including locoregional recurrence and distant	

multicenter study Number of Patient: 141 patients Recruitung Phase: 1992-2014 Inclusion Criteria: Patients with salivary duct carcinoma (SDC) without distant metastasis at initial diagnosis who underwent curative treatment as the initial treatment. Exclusion Criteria: -	- nerve preservation and nerve resection. Comparison: see intervention.	metastasis. Results: Patient characteristics (119 men (84.4%) and 22 women (15.6%). The primary tumor site was: - parotid gland in 112 patients (79.4 %), - submandibular gland in 25 (17.7 %), - minor salivary gland in 3 (2.1 %), - sublingual gland in 1 (0.7 %). Approximately two-thirds of the patients (93 patients, 66.0 %) presented with a T3/T4 tumor. Procedure: - 83 patients underwent surgery followed by adjuvant radiotherapy or chemoradiotherapy, - 51 patients underwent surgery alone, a - 7 patients received adjuvant chemotherapy without radiotherapy. Surgical procedures were: - extended total parotidectomy 31 patients, - total parotidectomy in 60, - partial parotidectomy (lobectomy) in 19, - parapharyngeal tumorectomy in 4, - submandibular gland resection in 25, - partial maxillectomy and extended sublingual gland resection in 1 each. The median follow-up period was 36 months. The 3- year OS and DFS rates were 70.5 % [95 % CI 61.4–77.8 %] and 38.2 % (95 % CI 29.5– 46.9 %), respectively. Independent prognostic factors for OS (multivariate analysis): - age ≥65 years [HR = 2.96, p<0.001, vs. <65 years]	

		- N1 and N2 (HR = 2.97 and 4.01, p = 0.047 and <0.001, respectively, vs. N0) and for DFS: - the primary sites of the minor salivary gland and sublingual gland (HR = 8.46, p<0.001, vs. the parotid gland) and - N2 (HR = 3.94, p<0.001, vs. N0). The most common treatment failure was distant metastasis (55 patients, 39.0 %). Partial Parotidectomy vs. Total Parotidectomy for Parotid SDC in the Early T Stage (33 patients): Univariate analysis, as well as multivariate analysis adjusted for age, sex, tumor size, N classification, rapid progression, pain, and adjuvant radiotherapy, showed no significant difference in OS, DFS, and LRC. Nerve Preservation vs. Nerve Resection (68 patients): Univariate analysis showed that OS, DFS, and LRC of the patients who underwent facial nerve resection were significantly worse than those whose facial nerves were preserved, however, in multivariate analysis no significant difference was found. Author's Conclusion: Our multi-institutional joint study revealed that advanced N stage independently affects both OS and DFS. Given the high incidence of distant failure, an effective systemic therapy is essential for improving DFS of SDC. Partial parotidectomy with facial nerve preservation may constitute a less invasive standard surgical procedure for parotid gland	

		SDC in the early T stage without facial nerve palsy.	
Methodical Notes			
Funding Sources: This study was supported in part by JSPS Grants-in-Aid for Scientific Research (C) to Y. Tada (No. 15K10823) and Y. Imanishi (No. 25462692). COI: None. Randomization: no. Blinding: no. Dropout Rate/ITT-Analysis: n.a. Notes: Oxford CEBM Level of evidence 2011: EL 4 (retrospective prognostic study)			
Park, G. C. et al. Clinically Node-Negative Parotid Gland Cancers: Prognostic Factors of Survival and Surgical Extent. Oncology. 98. 102-110. 2020			
Population	Intervention	Outcomes/Results	
Evidence level: 4 Study type: Retrospective, prognostic study. Number of Patient: 256 patients with cN0 parotid cancers. Recruitung Phase: March 1994 and December 2014. Inclusion Criteria: Patients who underwent surgery for primary parotid cancers included in the database of the Asan Medical	Intervention: 110 underwent conservative parotidectomy, and 146 underwent total parotidectomy. Comparison: see intervention	Primary: Recurrence-free survival (RFS) and overall survival (OS). Secondary: see primary. Results: Patient characteristics: - 50% male - median age 50 years (range 8-52) - 173 (67.6%) had T1–T2 tumors while 83 (32.4%) had T3–T4 tumors.	

center. Exclusion Criteria: Patients who had previously undergone surgery or received chemotherapy and/or radiotherapy for other cancers were excluded, as were patients with clinically node-positive (cN+) parotid cancers, distant metastases, or inoperable disease at initial diagnosis. Other exclusion criteria included referral for treatment of recurrent carcinomas in the parotid gland or neck, non-salivary gland tumors, metastatic carcinomas to the parotid gland, and incomplete data or follow-up.		Surviving patients were followed up for a median of 95 months (range 24–282). OS and RFS: The Kaplan-Meier estimates of 5-year RFS and OS rates were 85.7 and 91.4%, respectively. Patients with salivary duct carcinomas showed the poorest RFS and OS rates (60.6 and 76.2%, p = 0.05 and <0.01, respectively). Prognostic factors (multivariate analysis)for both RFS and OS: - a high histologic grade (HR 2.003 and 10.238, 95% CI 1.015–3.953 and 1.271–5.405; p = 0.045 and 0.009), - advanced T classification (T3–T4; HR 4.000 and 4.323, 95% CI 1.902–8.415 and 1.916–9.753; both p < 0.001), and - positive resection margin (HR 3.017 and 2.920, 95% CI 1.570–5.798 and 1.481–5.756; p = 0.007 and 0.002). Extent of Parotidectomy: Postoperative facial nerve paralysis was significantly more common in patients who underwent total parotidectomy (36.7 vs. 3.9%, p < 0.001, 201 patients low- or intermediate-grade cancers). The 5-year RFS and OS after conservative parotidectomy (93.7 and 100%, respectively) were not worse than those after total parotidectomy (85.5 and 90.9%, respectively; p =	

		0.033 and 0.020). Author's Conclusion: We have shown that the histological grade, status of resection margin, and T classification may be useful in stratifying survival and recurrence risks in patients with cN0 parotid gland cancers. Conservative parotidectomy may be safe for selected early T1–2 cN0 low- or intermediate-grade tumors if a resection margin is secured.	
Methodical Notes			
Funding Sources: This work was supported by a National Research Foundation of Korea (NRF) grant, funded by the Ministry of Science and ICT (MSIT), the Government of Korea (No. 2019R1A2C2002259, J.- L.R.; No. 2017017687, G.C.P.). COI: nothing to declare Randomization: No. Blinding: No. Dropout Rate/ITT-Analysis: n.a. Notes: Oxford CEBM Level of evidence 2011: EL 4 (retrospective, prospective study).			
Park, W. et al. Clinical outcomes and management of facial nerve in patients with parotid gland cancer and pretreatment facial weakness. Oral Oncol. 89. 144-149. 2019			
Population	Intervention	Outcomes/Results	

Evidence level: 4 Study type: Retrospective, prognostic study. Number of Patient: 45 patients Recruitung Phase: 1998 to 2017 Inclusion Criteria: Patients with malignant parotid gland cancer and facial weakness at presentation registered in the salivary gland registry Department of Otorhinolaryngology-Head & Neck Surgery, Seoul. Exclusion Criteria: -	Intervention: - complete tumor resection (parotidectomy) and facial nerve sacrifice without nerve reconstruction (n = 15), - complete tumor resection, facial nerve sacrifice with nerve graft (sural nerve graft) (n = 11), - complete surgery with facial nerve preservation (n = 5) and - primary non-surgical treatments (n = 12). Because the parotid mass with facial weakness highly suggested the parotid gland malignancy, all patients had pre-operative cytology (or core needle biopsy) diagnosis, radiological work-ups for parotid lesions and neck, and a screening test for systemic metastasis. Comparison: see intervention.	Primary: Progression-free survival and overall survival. Secondary: oncological status: - no evidence of disease, - alive with disease (loco-regional or distant disease), and - death of disease (there was no death from other causes). Facial weakness was scored with the House-Brackmann grading system for facial paralysis: - incomplete (House-Brackmann grades 1–4) and - complete facial weakness (grades 5–6). In incomplete facial weakness, the dysfunctional subsites (forehead, eye and lip) were also reviewed. Results: Patient characteristics: - Median follow-up was 20 months (range: -178 months). - We performed neck dissection in 22 patients: elective lymph node dissection in 11 and therapeutic lymph node dissection in 11. - cases diagnosed as N0 were 53.3% and N(+) were 46.6% - most parotid gland cancers causing facial weakness were advanced tumor stage and high-grade tumors. - Complete facial paralysis (House-Brackmann grades 5–6) was observed in 40% of patients at presentation. Incomplete facial weakness (House-Brackmann grades 2–4) or paralysis on specific face subsites was observed in 60% of patients.	

		OS and DF Overall and progression-free survival rates among all patients were 67.2% and 44.0% at 3 years, 40.1% and 38.5% at 5 years, respectively. - the group with initial non-surgical treatment showed the worst survival outcomes. - the two groups who underwent surgery and facial nerve sacrifice with or without nerve graft had similar oncological outcomes - The group with surgery and facial nerve preservation showed the best outcomes. Prognostic factors : tumor size and tumor grade were not significant prognosticators for survival. Metastasis (lymph node or distant sites) was a significant risk factor for worse survival. Multivariable analysis revealed no potential interaction between tumor grade and lymph node metastasis. Functional outcomes of facial weakness: - Facial nerve graft didn't improve facial nerve function. - Cases with facial nerve preservation during surgery had the best functional outcomes in terms of the facial expression. - In cases with nerve resection, 26.9% had intra-neural tumor invasion, 42.3% had perineural invasion, and 30.8% had no neural invasion in the FN. Author's Conclusion: In conclusion, a large portion (86.7%) of parotid gland cancers with facial weakness was high-grade tumors. Patients had poor clinical outcomes (44.0%	

		in 3Y progression-free survival) and approximately half of patients suffered recurrence. Recovery of facial weakness was suboptimal in patients with facial nerve graft, due to short disease-free intervals, that did not allow enough time for facial nerve recovery. Thus, static techniques for facial reanimation may be more desirable for these patients. In cases with incomplete facial weakness and safe separation of nerve from tumors, facial nerve preservation offered the best functional outcomes, without compromising oncological outcomes.	
Methodical Notes			
Funding Sources: This work was supported by a grant of the National Research Foundation of Korea (NRF) funded by the Korea government (MEST) (No. 2018R1A2B6002920). COI: Nothing to declare. Randomization: No Blinding: No Dropout Rate/ITT-Analysis: n.a. Notes: Oxford CEBM Level of evidence 2011: EL 4 (retrospective, prognostic study).			
Terakedis, B. E. et al. The Prognostic Significance of Facial Nerve Involvement in Carcinomas of the Parotid Gland. Am J Clin Oncol. 40. 323-328. 2017			
Population	Intervention	Outcomes/Results	
Evidence level: 4	Intervention: All patients in this series underwent surgery as the	Primary: Disease recurrence and survival.	

Study type: Retrospective chart review Number of Patient: 129 consecutive patients. Recruitung Phase: 1988 to 2006 Inclusion Criteria: Patients with previously untreated, nonmetastatic primary parotid gland malignancies underwent therapeutic surgery at the University of Utah and at Intermountain Healthcare, Salt Lake City, Utah. Patients with distant metastatic disease at the time of diagnosis, as well as those with parotid lymphoma. Exclusion Criteria: -	primary treatment modality. Parotid gland surgery was either a superficial or total parotidectomy. Comparison: -	Secondary: - Results: Patient characteristics: - Median follow-up was 72 months (range, 2.5 to 241 mo) - median age at diagnosis was 53 years (range, 9 to 94 y) - he majority of patients had T1/T2 tumors (66%) and - nodenegative disease (81%) - the number of patients undergoing superficial (n = 61) versus total parotidectomy (n = 68) were similar - of the 129 patients in this analysis, 86 (67%) received adjuvant RT. DFS and OS: - Five-year DFS was 79% for all patients. - Disease recurrence occurred in 32 (25%) patients, including 28 in the adjuvant RT group. - Distant recurrences were more common than locoregional recurrences - with lung followed by bone being the most predominant sites of distant failure. - age, histology, and FN sacrifice were significant predictors of poor OS (multivariate analysis) - Five-year and 10-year OS rates for the entire group were 78% and 67%, respectively. - Histology, age 60 years and above, and FN sacrifice remained statistically significant predictors of worse OS. FN involvement: Disease recurrence occurred in 64% of patients with both FN palsy and PNI, in 43% with FN palsy without PNI, in	

		27% with only PNI, and in 16% without either feature. Author's Conclusion: FN involvement is a predictor of increased risk of recurrence and death from parotid cancer. FN palsy seems to be a stronger predictor than PNI; however, PNI without FN palsy is associated with an elevated absolute risk of recurrence despite the use of postoperative RT in most patients. Postoperative RT seems to provide a benefit in patients with high-risk features, and in patients treated with adjuvant RT, distant failure becomes an increasingly important therapeutic issue. Although RT plays an important role in obtaining locoregional control, adjuvant RT does not seem to substitute for FN sacrifice in high-risk patients. Adjuvant chemotherapy has been associated with a mixed response, and further studies are evaluating the benefit of systemic treatment in high-risk patients.	
Methodical Notes			
Funding Sources: n.a. COI: Nothing to declare. Randomization: none. Blinding: none. Dropout Rate/ITT-Analysis: n.a. Notes: Oxford CEBM Level of evidence 2011: EL 4 (retrospective, prognostic study).			

Terhaard, C. et al. Facial nerve function in carcinoma of the parotid gland. European Journal of Cancer. 42. 2744-2750. 2006		
Population	Intervention	Outcomes/Results
Evidence level: 4 Study type: Retrospective, prognostic study. Number of Patient: 332 patients treated for a salivary gland carcinoma of the parotid gland. Recruitung Phase: 1985 to 1994 Inclusion Criteria: Patients obtained from all the participating centres of the Dutch Head and Neck Oncology Co-operative Group (NWHHT)and treated for a salivary gland carcinoma of the parotid gland. Exclusion Criteria: -	Intervention: Treatment consisted of - surgery alone in 11%, - surgery combined with postoperative radiotherapy in 77%, - radiotherapy alone in 8%, - chemotherapy alone in 2 patients and - chemotherapy followed by surgery and radiotherapy in another 2 patients, - no treatment was given to 11 patients (3%). For local surgical treatment - local excision was performed in 5%, - superficial parotidectomy in 30%, - total parotidectomy with preservation of the facial nerve in 43% and - with sacrifice of the facial nerve in 21%. Comparison: -	Primary: Prognostic factors, DFS, facial nerve function. Secondary: - Results: Patient characteristics: - the mean follow-up of patients alive at last follow-up was 98 months. - mean age was 60 years (range 8-100 years) - data concerning facial nerve function were available in 324 patients - in 67% the tumour was located in the lateral lobe - 85% of all cases were N0 stage The function of the facial nerve before treatment was: - intact in 77% (n = 255), - partially impaired in 14% (n = 45) and - complete paralysis was noted in 7% (n = 24). Correlation between facial nerve function before treatment and patient and tumour characteristics: Independent prognostic factors were: - localisation, with a high risk of dysfunction for tumours originating from the medial lobe, - N-stage, - pain and

		- age Perineural invasion was the only independent correlating factor for nerve facial function. Local-regional control: Independent prognostic factors: - treatment applied ($p < 0.0001$), - age ($p = 0.03$, younger patients fared better) and - clinical T-stage. - Postoperative radiotherapy increased local control ($p < 0.001$). - Bone invasion ($p = 0.001$) and status of the resection margins ($p = 0.05$) were additional independent prognostic factors ($p = 0.001$). Distant metastases free survival: Distant metastases were seen in 23%, 39% and 57%, respectively, for normal, partially impaired and complete by paralysed facial nerve ($p = 0.001$). Disease free survival: Percentage disease free survival was 69, 37 and 13, respectively, for normal, partially impaired and completely paralysed facial nerve ($p < 0.001$). In multivariate analysis, clinical T-stage ($p = 0.004$), treatment ($p < 0.001$) and pre-treatment function of the facial nerve ($p = 0.03$) were independent variables. Facial nerve function:	

		After treatment 22% of the patients experienced a partial paralysis, and 13% of the patients experienced a complete parlysis of N VII. Author's Conclusion: For patients with parotid carcinoma, facial nerve function before treatment is a strong prognostic factor for disease free survival	
Methodical Notes			
Funding Sources: not specified. COI: Nothing to declare. Randomization: No. Blinding: No. Dropout Rate/ITT-Analysis: n.a. Notes: Oxford CEBM Level of evidence 2011: EL 4 (Retrospective, prognostic study).			