Author’s response to reviews

Title: Incidence of postoperative facial weakness in parotid tumor surgery: A tumor subsite analysis of 794 parotidectomies

Authors:

Hokyung Jin (hk.jin.life@gmail.com)
Bo Young Kim (by0131@gmail.com)
Heejung Kim (hj0823.kim@samsung.com)
Eunkyu Lee (eunkyu2.lee@samsung.com)
Woori Park (woori.park@samsung.com)
Sungyong Choi (sungyong82.choi@samsung.com)
Man Ki Chung (manki.chung@samsung.com)
Young-Ik Son (yison@skku.edu)
Chung-Hwan Baek (chbaek@skku.edu)
Han-Sin Jeong (hansin.jeong@gmail.com)

Version: 1 Date: 02 Dec 2019

Author’s response to reviews:

AUTHOR RESPONSE

RE: BSUR-D-19-00402 (BMC SURGERY)
Incidence of postoperative facial weakness in parotid tumor surgery: A tumor subsite analysis of 794 parotidectomies

Dear Editors and Reviewers,

Thank you for kind consideration of this article. We corrected it point-by-point and revised the manuscript following your recommendations. Corrected parts are marked with highlight (in highlighted version). We would be happy if the revised manuscript is more suitable to publication in the BMC SURGERY.

Best regards,

Han-Sin Jeong, the corresponding author of BSUR-D-19-00402.
POINT-BY-POINT RESPONSE

Editor Comments:

Please include a cover letter with a point-by-point response to the comments, describing any additional experiments that were carried out and including a detailed rebuttal of any criticisms or requested revisions that you disagreed with. Please also ensure that all changes to the manuscript are indicated in the text by highlighting or using track changes.

Answer: Thank you for instructions. This is a point-by-point author response to the issues raised by the reviewers. We also provided the revised manuscript, in which the corrections are highlighted.

Reviewer reports:

Maria Grosheva (Reviewer 1):
The authors analyze the incidence for the facial palsy after parotidectomy for benign and malignant lesions. In their retrospective analysis, they include 794 parotidectomies during a 7 year time period from a single institution. This corresponds to approximately 113 surgeries per year and indicates a very good expertise in parotid surgery.

Besides the retrospective nature of the study, I would like to address another methodological weak point of the manuscript. The authors cannot include parotidectomy for malignant tumors in their analysis, because it will substantially bias the outcome of the primary objective of the study. In 21 patients, a radical parotidectomy was performed because of peri-neural infiltration. Even if only patients with a malignant tumor and preserved facial nerve would be included, this would still significantly influence the statistics: These patients might be elder than the standard patients with a benign lesion; most of the patients with a malignant lesion would undergo a total parotidectomy, which takes significantly longer than usual.

Answer: This is a very good point, and thank you for your question.

The aim of this study was to re-evaluate the risk (incidence) of facial weakness in patients who had undergone a surgery for parotid tumors, not limited to the benign tumors. In concordance with the reviewer’s comment, the risk of facial weakness in parotidectomy for malignant tumors was higher than that of benign tumor parotidectomy in our series (21.7% vs. 6.5% in temporary, 14.4% vs. 3.4% in permanent facial weakness).

However, we did not exclude 143 malignant tumors (who had intact facial function preoperatively) in the revised version of the manuscript. The reasons are summarized as follows.

The primary aim of this study was to provide up-to-date information about the incidence of facial weakness in parotidectomy for patient counseling (Introduction). The problem in preoperative diagnosis of parotid gland tumors is that the discrimination between benign and malignant tumors could not be clear, preoperatively, even with the multiple diagnostic tools. In some cases, the pathological diagnosis of malignant parotid tumors can only be achieved after the detailed examination of surgical pathology.
Thus, information about a risk of facial weakness in parotidectomy for both benign (majority) and malignant tumors (intact facial nerve) would be helpful for patient counseling, even though we strongly agree with higher incidence of facial weakness in surgery for malignant tumors.

Another thing to note is that the extent of surgery seems to be overlapped between the benign tumors and low-grade malignant tumors nowadays.

(References)

In our retrospective series, we found that the extent of surgery was significantly correlated with tumor pathology ($P < 0.001$) (malignant tumors or not), which was essentially in agreement with the reviewer’s comment. Nevertheless, we think that the current analysis of our series could have some benefits to give information for patients with unknown malignant potentials at surgery.

Detailed review of the manuscript:

The Abstract should be shortened. Especially, the first paragraph is expendable. The authors should focus on the aim of the study.

Answer: Thank you for your comments.
We rewrote the Abstract section, focusing on the aim of the study.

Abstract
Background
The reported incidence of facial weakness immediately after parotid tumor surgery ranges from 14% to 65%. The purpose of this study was to evaluate the incidence of postoperative facial weakness related to parotidectomy with use of preoperative computed tomography, intraoperative facial nerve monitoring, and surgical magnification. Also, we sought to elucidate additional information about risk factors for postoperative facial weakness in parotid tumor surgery, particularly focusing on the tumor subsites.

Methods
We retrospectively reviewed 794 cases with parotidectomy for benign and malignant tumors arising from the parotid gland (2009–2016). Patients with pretreatment facial palsy were excluded from the analyses. Tumor subsites were stratified based on their anatomical relations to the facial nerve as superficial, deep, or both. Multivariable logistic regression analyses were conducted to identify risk factors for postoperative facial weakness.

Results
The overall incidences of temporary and permanent (more than six months) facial weakness were 9.2% and 5.2% in our series utilizing preoperative CT, intraoperative facial nerve monitoring, and surgical
magnification. Multivariable analysis revealed that old age, malignancy, and recurrent tumors (revision surgery) were common independent risk factors for both temporary and permanent postoperative facial weakness. In addition, tumor subsite (tumors involving superficial and deep lobe) was associated with postoperative facial weakness, but not tumor size. Extent of surgery was strongly correlated with tumor pathology (malignant tumors) and tumor subsite (tumors involving deep lobe).

Conclusion
Aside from risk factors for facial weakness in parotid tumor surgery such as old age, malignant, or recurrent tumors, the location of tumors was found to be related to postoperative facial weakness. This study result may provide background data in a future prospective study and up-to-date information for patient counseling.

The purpose of the CT- scan is unclear throughout the manuscript. Moreover, worldwide an ultrasound and the MRI are the imaging methods of choice for preoperative diagnostics for parotid tumors. Preoperative imaging is crucial for careful selection of patients for more or less extensive surgery (ECD, partial parotidectomy, total parotidectomy), and in several cases, might indicate malignancy. Either way, the presence of a CT scan will not prevent complications after parotidectomy (especially not the incidence of the facial nerve palsy).

Answer:

We, the authors, totally agree with the reviewer’s comment on the diagnostic role of CT in parotid gland tumors. In the revised version, we put little emphasis on CT scan through the manuscript, and discussed further limitation of CT in the management of parotid gland tumors. Thank you for your invaluable comments.

Corrections:

Abstract
Conclusion
Aside from risk factors for facial weakness in parotid tumor surgery such as old age, malignant, or recurrent tumors, the location of tumors was found to be related to postoperative facial weakness. This study result may provide background data in a future prospective study and up-to-date information for patient counseling.

Background

In this study, we routinely applied preoperative computed tomography (CT) scans, intraoperative facial nerve monitoring, and surgical magnification for all parotidectomies, which is different from the previous studies. Preoperative CT scans is known to have a modest diagnostic accuracy for localization of parotid tumors in relation to the facial nerve using an imaginary facial nerve on images (Ref). Thus, CT scans have some diagnostic limitations compared with the direct visualization of the facial nerve by advanced techniques of magnetic resonance imaging (MRI) (Ref). However, preoperative CT could provide the gross characteristics of tumors in the parotid gland, approximate location of tumors, and sketchy surgical planning. More importantly, CT scans can be cost-effective and more popular in many countries, compared with the specialized MRI techniques. Combined with intraoperative facial nerve
monitoring and surgical magnification, the surgeons may capture an advantageous position in functional preservation of the facial nerve during parotidectomy.

Reference (Add)


Methods

Preoperative imaging and intra-operative facial nerve monitoring

All subjects preoperatively underwent CT with contrast enhancement and fine needle aspiration cytology (ultrasonography-guided if indicated). CT scans were performed with non-contrast axial view (14.5 mm thickness), contrast-enhanced axial view (8 mm thickness) and contrast-enhanced coronal view (3.6 mm thickness). Additional imaging studies for tumor characterization and metastasis evaluation were conducted for patients with parotid tumors suspicious for malignancy (positron emission tomography and magnetic resonance imaging).

Tumor subsites were categorized into three compartments based on the surgical findings (anatomical relationship to the facial nerve) as follows: superficial to the facial nerve, deep to the facial nerve and tumors located in both the superficial and deep lobes crossing the facial nerve plane.

Discussion, Line 272

In the present study, preoperative CT allowed us to estimate the positional relationship between the imaginary facial nerve line and the tumor before surgery. However, this indirect method on CT images showed only a modest diagnostic accuracy for localization of parotid tumors in relation to the facial nerve (Ref). Thus, the tumor subsites in this study were classified based on the surgical findings, not on the CT images. Recent advanced techniques of magnetic resonance imaging may have clinical benefit of more accurate surgical planning by directly visualizing the facial nerve in the parotid gland (Ref).

Reference (Add)


With the aid of intraoperative nerve monitoring and surgical magnification, the anatomical continuity of the facial nerve could be preserved, even with rerouting of the facial nerve during surgery for tumors located in both the superficial and deep lobes. Although temporary facial weakness might be caused by excessive manipulation of the facial nerve, rates of permanent facial weakness seemed not to be high due to preservation of the nerve continuity and recovery of the facial nerve conduction.
Background/ Introduction (page 5):

Similar to the abstract, the facts in the first paragraph are much generalized. The authors should focus on the aim of their study and explain why another clarification of the risk factors is needed.

Answer:
We condensed the first paragraph of Background section, and more focused on the aim of the study.

Corrections:

Background (Revised)

Functional preservation of the facial nerve in the affected gland is one of the most essential surgical steps in parotidectomy [1, 2]. To identify and preserve the facial nerve safely, many surgical landmarks have been proposed to locate the facial nerve consistently during parotidectomy [3-5]. In addition, preoperative imaging tests, intraoperative electromyographic monitoring of the facial nerve and use of a magnified surgical view (surgical loupes or microscope) have emerged as routine clinical steps in parotidectomy [6-13].

According to previous studies, 14% to 64% for temporary and 0% to 9% for permanent facial nerve weakness have been reported following parotidectomy [2, 10, 13-21]. Furthermore, much higher rates of facial nerve paresis were observed for revision parotid surgery [16, 22, 23], wide extent of surgery (total parotidectomy) [15, 16, 22-26], tumor located deeper than the facial nerve plane [17, 27], and in cases with large tumors [25, 28-30]. Recent studies also reported the improved rates of functional facial nerve preservation in parotidectomy, with the aid of preoperative imaging tests, intraoperative monitoring of the facial nerve, or surgical magnification [31-36]. Still there have been no strong evidence to support the preventive role of intra-operative facial nerve monitoring from facial nerve injury during parotidectomy. However, several studies suggested that rates of temporary or permanent facial palsy could be decreased in parotidectomy with intra-operative facial nerve monitoring [13, 14, 17, 25, 35].

In this study, we routinely applied preoperative computed tomography (CT) scans, intraoperative facial nerve monitoring, and surgical magnification for all parotidectomies, which is different from the previous studies. Preoperative CT scans is known to have a modest diagnostic accuracy for localization of parotid tumors in relation to the facial nerve using an imaginary facial nerve on images [37]. Thus, CT scans have some diagnostic limitations compared with the direct visualization of the facial nerve by advanced techniques of magnetic resonance imaging (MRI) [37]. However, preoperative CT could provide the gross characteristics of tumors in the parotid gland, approximate location of tumors, and sketchy surgical planning. More importantly, CT scans can be cost-effective and more popular in many countries, compared with the specialized MRI techniques. Combined with intraoperative facial nerve monitoring and surgical magnification, the surgeons may capture an advantageous position in functional preservation of the facial nerve during parotidectomy.

Thus, the purpose of this study was to evaluate the incidence of postoperative facial weakness related to parotidectomy with use of preoperative CT scans, intraoperative facial nerve monitoring, and surgical magnification. Also, we sought to identify risk factors for facial nerve palsy, particularly focusing on tumor subsites, which has been less studied. This study will provide background data in a future prospective study and up-to-date information for patient counseling.
During the last years, the incidence of the facial nerve palsy during parotidectomy, especially for benign tumors, decreased substantially because of the excellent standardization of the surgical technique, use of the microscope or a loupe and a facial nerve monitoring. For this reason, the incidences which were reported in the 80-ies and 90-ies are more than outdated. The authors refer altogether to 19 studies which were published prior to 1990 throughout the manuscript. These is excellent research in due course. However, several manuscripts with high level of evidence and meta-analyses have been published since then, which present the current data more precise.

Answer:
We updated the references with recently published articles (2012-2019) according to the reviewer’s comment. Thank you for your comments.

Corrections:
References added


Again, the use of the preoperative CT scan is unclear to me. On lines 87 and following, the authors criticize the lack of preoperative imaging. As previously mentioned, the use of a CT scan is not standard of care for parotid tumors.

Answer: Thank you for your comments.

We agree with the reviewer’s comment on the diagnostic role of CT in parotid gland tumors. In the revised version, we put little emphasis on CT scan through the manuscript, and discussed further limitation of CT in the management of parotid gland tumors.
Background

In this study, we routinely applied preoperative computed tomography (CT) scans, intraoperative facial nerve monitoring, and surgical magnification for all parotidectomies, which is different from the previous studies. Preoperative CT scans is known to have a modest diagnostic accuracy for localization of parotid tumors in relation to the facial nerve using an imaginary facial nerve on images (Ref). Thus, CT scans have some diagnostic limitations compared with the direct visualization of the facial nerve by advanced techniques of magnetic resonance imaging (MRI) (Ref). However, preoperative CT could provide the gross characteristics of tumors in the parotid gland, approximate location of tumors, and sketchy surgical planning. More importantly, CT scans can be cost-effective and more popular in many countries, compared with the specialized MRI techniques. Combined with intraoperative facial nerve monitoring and surgical magnification, the surgeons may capture an advantageous position in functional preservation of the facial nerve during parotidectomy.

Reference (Add)


Methods

Preoperative imaging and intra-operative facial nerve monitoring
All subjects preoperatively underwent CT with contrast enhancement and fine needle aspiration cytology (ultrasonography-guided if indicated). CT scans were performed with non-contrast axial view (14.5 mm thickness), contrast-enhanced axial view (8 mm thickness) and contrast-enhanced coronal view (3.6 mm thickness). Additional imaging studies for tumor characterization and metastasis evaluation were conducted for patients with parotid tumors suspicious for malignancy (positron emission tomography and magnetic resonance imaging).

Tumor subsites were categorized into three compartments based on the surgical findings (anatomical relationship to the facial nerve) as follows: superficial to the facial nerve, deep to the facial nerve and tumors located in both the superficial and deep lobes crossing the facial nerve plane.

Discussion

In the present study, preoperative CT allowed us to estimate the positional relationship between the imaginary facial nerve line and the tumor before surgery. However, this indirect method on CT images showed only a modest diagnostic accuracy for localization of parotid tumors in relation to the facial nerve (Ref). Thus, the tumor subsites in this study were classified based on the surgical findings, not on the CT images. Recent advanced techniques of magnetic resonance imaging may have clinical benefit of more accurate surgical planning by directly visualizing the facial nerve in the parotid gland (Ref).

Reference (Add)

Localization of Parotid Gland Tumors in Relation to the Intraparotid Facial Nerve on 3D Double-Echo
Additionally, the use of the EMG facial nerve monitoring is discussed (lines 89 ff). Whereas its use is worldwide accepted, there is no statistical evidence of its additional advantage for prevention of the facial nerve palsy, if applied to optical facial nerve monitoring. The authors should clarify this.

Answer:
We agree on this point with the reviewer.
Still there have been no strong evidence to support the preventive role of intra-operative facial nerve monitoring from facial nerve weakness during parotidectomy. However, one meta-analysis study pointed out that intra-operative facial nerve monitoring could decrease the rate of temporary facial weakness in primary parotidectomies (Ref).

Reference

The report is in agreement with our findings: (Line 240-242) a tumor factor rather than surgical technique may be a major determinant of permanent facial weakness. We think that intra-operative facial nerve monitoring combined with proper surgical planning and surgical magnification could decrease the facial nerve injury by technical problems.

We clarified this issue in the revised manuscript.

Corrections:
Background
Still there have been no strong evidence to support the preventive role of intra-operative facial nerve monitoring from facial nerve injury during parotidectomy. However, several studies suggested that rates of temporary or permanent facial palsy could be decreased in parotidectomy with intra-operative facial nerve monitoring [13, 14, 17, 25, 35].

Discussion
Even with intraoperative facial nerve monitoring, the frequency of temporary facial weakness was within a similar range (20.0%-33.3%) [13, 14, 17, 25]; meanwhile, permanent facial weakness was less frequently seen, ranging from 0.0% to 9.0% after parotidectomy [13, 14, 17, 19, 25]. In contrast, one meta-analysis reported that intra-operative facial nerve monitoring could not decrease the rate of permanent facial weakness in primary parotidectomies [35].

On lines 94, the authors claim that the location of the tumor in reference to the facial nerve, might be predicted by preoperative imaging. To my opinion, this is only applicable for large deep lobe tumors. The true localization of a standard lesion is only visible during surgery.

Answer:
In this study, the tumor location (tumor subsite) was determined in reference to the facial nerve, based on the surgical findings. We clarified it and corrected the text accordingly.
Abstract
We retrospectively reviewed 794 cases with parotidectomy for benign and malignant tumors arising from the parotid gland (2009–2016). Patients with pretreatment facial palsy were excluded from the analyses. Tumor subsites were stratified based on their anatomical relations to the facial nerve as superficial, deep, or both. Multivariable logistic regression analyses were conducted to identify risk factors for postoperative facial weakness.

Methods
Tumor subsites were categorized into three compartments based on the surgical findings (anatomical relationship to the facial nerve) as follows: superficial to the facial nerve, deep to the facial nerve and tumors located in both the superficial and deep lobes crossing the facial nerve plane.

Answer:
The aim of this study was to re-evaluate the risk (incidence) of facial weakness in patients who had undergone a surgery for parotid tumors, not limited to the benign tumors. In concordance with the reviewer’s comment, the risk of facial weakness in parotidectomy for malignant tumors was higher than that of benign tumor parotidectomy in our series (21.7% vs. 6.5% in temporary, 14.4% vs. 3.4% in permanent facial weakness).

However, we did not exclude 143 malignant tumors (who had intact facial function preoperatively) in the revised version of the manuscript. The reasons are summarized as follows.

The primary aim of this study was to provide up-to-date information about the incidence of facial weakness in parotidectomy for patient counseling (Introduction). The problem in preoperative diagnosis of parotid gland tumors is that the discrimination between
benign and malignant tumors could not be clear, preoperatively, even with the multiple diagnostic tools. In some cases, the pathological diagnosis of malignant parotid tumors can only be achieved after the detailed examination of surgical pathology.

Thus, information about a risk of facial weakness in parotidectomy for both benign (majority) and malignant tumors (intact facial nerve) would be helpful for patient counseling, even though we strongly agree with higher incidence of facial weakness in surgery for malignant tumors.

Another thing to note is that the extent of surgery seems to be overlapped between the benign tumors and low-grade malignant tumors nowadays.

(References)

In our retrospective series, we found that the extent of surgery was significantly correlated with tumor pathology (P &lt; 0.001) (malignant tumors or not), which was essentially in agreement with the reviewer’s comment. Nevertheless, we think that the current analysis of our series could have some benefits to give information for patients with unknown malignant potentials at surgery.

Page 7, Lines 127-128: Was 2 or 4 channel EMG Monitoring applied?

Answer: We supplemented it in detail. The intra-operative facial nerve monitoring system was a NIM-Response 2.0 with four channel monitoring (Medtronic, Minneapolis, MN, USA)

Page 7, line 138 and following: extra-capsular dissection should be changed to extracapsular dissection (ECD).

Answer: We corrected it according to the reviewer suggestion.

Page 8, lines 151 and following: To my opinion, the facial dysfunction after 6 months still might improve. The authors should clarify why the facial dysfunction after 6 months was defined as a permanent palsy. Furthermore, it would be interesting in which patents with a palsy at 6 months the palsy was permanent and still present at 12 months.

Answer: Thank you for asking an important issue. We agree with the reviewer on this point. The time-points for facial nerve functions were postoperative day 1 to 5 and 6 to 12 months. The facial weakness of one or more facial subsites at 6 to 12 months after parotidectomy was defined as permanent facial palsy in this study (previously described in the Method section).

The patients with temporary facial palsy, but with the intact anatomical facial nerve continuity were followed up to 12 months. However, when the facial nerve was sacrificed at the time of parotidectomy, it was diagnosed as permanent facial palsy at the time-point of postoperative 6 months. Further improvement of facial expression after 6 months in patients with resected facial nerve appeared to be a result of aberrant regeneration or compensation.
These explanations were added in the Method section.

Results (pages 8ff).
The data is well presented in four tables. Accordingly, the information, especially regarding the patients characteristics is redundant. I suggest to shorten the first paragraph.

Answer:
Thank you for comments. We condensed the first paragraph of the Result section.

Corrections:
Results
Subject characteristics
A total of 794 patients were included in this study (Table 1). The histopathology revealed that 651 patients had benign tumors (82.0%) and 143 patients had malignant tumors (18.0%) (Additional file: Table S1).

Page 9, Lines 178 following: The whole paragraph is somehow illogical and confusing. In the first sentence the number of patients with a palsy after 12 months is missing. Then, the rates for primary surgery are shown. In the following, the authors describe the increased (?) incidence of the temporary palsy after revision surgery, malignant tumors and in deep lobe tumors. It would be nice to focus on a few corner points / specific data and to present it more clearly. Otherwise, it looks like random enumeration.

Answer:
Thank you for your comments. We rephrased the paragraph and clarified it.

Corrections:
Results
Subject characteristics
A total of 794 patients were included in this study (Table 1). The histopathology revealed that 651 patients had benign tumors (82.0%) and 143 patients had malignant tumors (18.0%) (Additional file: Table S1).

Among total patients, 73 patients (9.2%) had temporary facial weakness and 41 patients (5.2%) had permanent facial weakness. Meanwhile, the rates of temporary and permanent facial weakness were 21.7% and 14.4% for malignancy, 29.8% and 19.3% for tumors located in both superficial and deep lobes, 33.0% and 20.5% for cases with total parotidectomy, and 26.8% and 19.5% for revision surgery. In 21 patients out of the 143 malignant tumors, some branches of the facial nerve were intentionally sacrificed to secure the safety margin during surgery. Seven of the 21 patients of whom the buccal and cervical branches of the facial nerve had been sacrificed during surgery, had no facial weakness at 6 months postoperatively.

Page 9, Line 189: I would rename into "Degree or Extent or Evaluation of facial dysfunction"

Answer:
We renamed the section as Degree of facial dysfunction, instead of Details of facial weakness.
Page 10, Lines 197 and following: For the analysis of the extent of surgery, the ECD and partial parotidectomy were merged. In several recent prospective trials could be shown, that ECD is associated with a significantly lower incidence of the facial nerve palsy compared to parotidectomy approached, which requires the dissection of the facial nerve (partial, superficial parotidectomy, etc.). For this reason, I strongly suggest to separate the ECD and the partial parotidectomy for this analysis.

Answer:
Thank you for comments.
As the reviewer’s comment, we re-analyzed the extent of surgery with 4 categorization of ECD, partial, superficial and total parotidectomy (Revised Table 3 and 4). We found that only total parotidectomy in extent of surgery had a significant negative impact on the occurrence of postoperative facial weakness.

Corrections:
Revised Table 3. Temporary facial weakness
Extent of surgery
ECD (Reference): 1
Partial parotidectomy: OR 2.675, 95%CI [0.625-11.444], P=0.185,
Superficial parotidectomy: OR 2.839, 95%CI [0.625-12.889], P=0.176,
Total parotidectomy: OR 18.678, 95%CI [4.283-81.455], P<0.001.

Revised Table 4. Permanent facial weakness
Extent of surgery
ECD (Reference): 1
Partial parotidectomy: OR 2.154, 95%CI [0.276-16.804], P=0.464,
Superficial parotidectomy: OR 4.350, 95%CI [0.574-34.578], P=0.165,
Total parotidectomy: OR 19.800, 95%CI [2.576-152.201], P=0.004.

Lines 208-209: It is only logical, that the extent of surgery is higher in treatment of malignant tumors and in cases where the tumor exceed the superficial lobe.

Answer:
Thank you for comments. We rewrote the sentence to give a meaning more clearly.

Corrections:
Results (line 208-209)
However, the extent of surgery was significantly bigger in cases with malignant tumors (P < 0.001) and in cases with deep lobe tumor or tumor crossing the nerve (P < 0.001), according to Pearson’s chi-square test. Thus, the extent of surgery variable was excluded in these multivariable analyses, due to the potential multicollinearity. The remaining variables within a multivariable model showed variance inflation factors of less than 2.0.

Lines 205 and 215: the reference to the Figures is missing

Answer:
We added appropriate references to the text.

Reference
Belsley D.A., Kuh E. and Welsch R.E. Detecting and Assessing Collinearity in Regression Diagnostics:
Discussion (Pages 11-13): The same, as in introduction: The incidence of the facial nerve palsy during parotidectomy, especially for benign tumors, decreased substantially during the last years, the incidence of the facial nerve palsy during parotidectomy, especially for benign tumors, decreased substantially because of the excellent standardization of the surgical technique, use of the microscope or a loupe and a facial nerve monitoring. For this reason, the incidences which were reported in the 80-ies and 90-ies are more than outdated. The authors refer altogether to 19 studies which were published prior to 1990 throughout the manuscript. These is excellent research in due course. However, several meta-analyses has been published since then, which present the current data more precise.

Answer:
We updated the references with recently published articles (2012-2019) according to the reviewer’s comment. Thank you for your comments.

Corrections:
References added


Lines 256-258: If I understand this correctly, the authors stated that the recovery of the facial nerve is delayed and/or insufficient in female patients? This is very far-fetched. I suggest, that the authors re-analyze the influencing factors for this outcome (maybe more malignant tumors? are there any independent research which would confirm this fact?)
Answer:
We re-analyzed the risk factor analysis (univariable and multivariable regression analysis, Table 4) and found that the female gender itself was not an independent risk factor for permanent facial weakness. Thus, we deleted those sentences in the revised version of manuscript.

Corrections:

Method
Using the variables with a significant P value (less than 0.05) in univariable analyses, we generated a multivariable model, in which final estimates for each would yield an adjusted odds ratio for each factor retained in the model.

Revised Table 4.

Gender: M vs. F (ref)
Univariable analysis OR=1.558, 95%CI [0.819-2.966], P = 0.177
Multivariable analysis: Gender variable was not included in the multivariable regression analysis (not significant).

Lines 274 and following: "The preoperative CT allows us to estimate the positional relationship between the imaginary nerve line and the tumor before surgery". I strongly disagree with this statement. The imaging of the peripheral facial nerve using the CT scan is not as far developed. There are some high-field-MRI studies regarding this matter though. For this reason, the following statement ("the anatomical continuity of the facial nerve could be preserved because of the accurate preoperative CT") is inaccurate, too.

Answer:
We totally agree with the reviewer’s comment on the diagnostic role of CT in parotid gland tumors. In the revised version, we deleted this sentence, and discussed further limitation of CT in the management of parotid gland tumors.

Corrections:

Discussion, Line 272-274
In the present study, preoperative CT allowed us to estimate the positional relationship between the imaginary facial nerve line and the tumor before surgery. However, this indirect method on CT images showed only a modest diagnostic accuracy for localization of parotid tumors in relation to the facial nerve (Ref). Thus, the tumor subsites in this study were classified based on the surgical findings, not on the CT images. Recent advanced techniques of magnetic resonance imaging may have clinical benefit of more accurate surgical planning by directly visualizing the facial nerve in the parotid gland (Ref).

Reference (Add)
With the aid of intraoperative nerve monitoring and surgical magnification, the anatomical continuity of the facial nerve could be preserved, even with rerouting of the facial nerve during surgery for tumors located in both the superficial and deep lobes. Although temporary facial weakness might be caused by excessive manipulation of the facial nerve, rates of permanent facial weakness seemed not to be high due to preservation of the nerve continuity and recovery of the facial nerve conduction.

In general, the manuscript should be linguistically edited. The sentences are often too long and confusing. For example, lines 64-66 (Abstract), lines 232-233, 240-242.

Answer:
We rephrased those sentences according to the reviewer's comments.

Corrections:

Abstract
Conclusion (Line 64-66)
Aside from risk factors for facial weakness in parotid tumor surgery such as old age, malignant, or recurrent tumors, the location of tumors was found to be related to postoperative facial weakness. This study result may provide background data in a future prospective study and up-to-date information for patient counseling.

(Line 232-233)
However, the surgical outcomes using these techniques have not been fully studied except for a few studies.

(Line 240-242)
Thus, a tumor factor rather than surgical technique may be a major determinant of permanent facial weakness.

Petros Konofaos, MD, PhD (Reviewer 2):
The authors evaluated the incidence of postoperative facial weakness related to parotidectomy with use of preoperative computed tomography (CT) scans, intraoperative facial nerve monitoring, and surgical magnification. Also, we sought to identify risk factors for facial nerve palsy, particularly focusing on tumor sub-sites, which could be predicted by preoperative imaging. The study is well-written and I think is suitable for publication in its current form.

Answer: Thank you so much for your positive comments.