ORIGINAL ARTICLE - PITUITARIES

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Use of intraoperative intracavitary (direct-contact) ultrasound for resection control in transsphenoidal surgery for pituitary tumors: evaluation of a microsurgical series

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Abstract

Background Perisellar infiltration may be responsible for incomplete removal of pituitary tumors. Since intraoperative visualization of parasellar structures is difficult during transsphenoidal surgery, we are describing the use of intraoperative direct contact ultrasound (IOUS).

Methods Within 5 years, in 113 transsphenoidal operations (58 male, 55 female, age 14–81 years, 110 pituitary adenomas (mean diameter 26.6 mm, 69 non-secreting adenomas, 41 secreting adenomas), and 1 of each Rathke's cleft cyst, craniopharyngioma, and xanthogranuloma), IOUS was applied. After wide opening of the sellar floor and removal of the intrasellar tumor portions, a commercially available side fire ultrasound probe is introduced, and in direct contact to the sellar envelope, the perisellar space is scanned perpendicular to the axis of the working channel. We compared the results of IOUS to postoperative MRI after 3–6 months.

Results Identification of the intracavernous ICA, the anterior optic pathway, and the ACA, was possible, it was safe to operate close to them. In 65 operations (58%), further resection of tumor remnants was performed after IOUS. In this selected series, complete resection of tumors (stated by postoperative MRI after 3–6 months) was achieved in 75 operations (66%) and remission was achieved in 18 operations of secreting adenomas (44%). Compared to MRI after 3 to 6 months, the sensitivity of IOUS was 0.568 and the specificity was 0.907. No complications related to IOUS were seen.

Conclusions Visualization of the perisellar compartments by IOUS is easy and fast to perform. It allows the surgeon to identify resectable tumor remnants intraoperatively, which otherwise could be missed.

Keywords Intraoperative ultrasound · Pituitary surgery · Transsphenoidal surgery · Pituitary tumor

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Abbreviations

ACA	Anterior cerebral artery
ACTH	Adrenocorticotropic hormone
ADH	Antidiuretic hormone
A1	A1-segment of ACA
CS	Cavernous sinus
CSF	Cerebrospinal fluid
CT	Computed tomography
GH	Growth hormone
ICA	Internal carotid artery
IGF-1	Insulin-like growth factor 1
IOUS	Intraoperative ultrasound
MRI	Magnetic resonance imaging
OC	Optic chiasm
ON	Optic nerve

PRL   Prolactin
SIADH   Syndrome of inappropriate ADH secretion
TSH   Thyroid-stimulating hormone

Introduction

Despite of widespread, either microsurgical or endoscopic use of the transsphenoidal approach, intraoperative visualization and complete resection of large pituitary adenomas remain a challenge, especially in case of parasellar tumor extension. Operations for large and infiltrating pituitary adenomas have a higher complication rate on the one hand and a lower resection rate on the other hand [5, 14, 16, 19, 21, 22, 28].

Many techniques were applied using guidance systems or intraoperative imaging to overcome this challenge. The application of navigation systems was evaluated in many studies. However, inaccuracy and intraoperative shift are limiting factors [10, 12, 32, 39]. The use of intraoperative CT was described but not established in the routine use [40]. The advantage of intraoperative MRI using low field techniques was described. The results of this technique improved after using high-field equipment [2, 6, 11, 13, 30, 35, 44]. The introduction of intraoperative ultrasound into transsphenoidal surgery was described in several studies. This technique was used for resection control as well as for detection of microadenomas [3, 4, 21, 24, 34, 38, 43, 45]. Solheim et al. described the use of a prototype of an ultrasound probe to detect tumor remnants and surrounding structures during transsphenoidal surgery in nine patients with pituitary adenomas [36].

Since the 1990s, many centers started to use the endoscopic technique in transsphenoidal surgery. Diverse techniques have been developed using pure endoscopic and endoscopic-assisted systems. This technique allows a panorama view of the sella. However, as in microsurgical technique, endoscopy allows the surgeon only to see the inner surface of the sellar compartment without detecting the structures hidden behind its walls. Studies comparing endoscopic and microscopic technique did not show one of them to be superior to the other [1, 7–9, 20, 26, 29, 41]. Combination of endoscopic technique with intraoperative ultrasound may provide a panorama view of the sella and help the surgeon to detect structures behind the surface of the surgical field [17, 31].

Here, we describe the use of intraoperative ultrasound (IOUS) with a commercially available, side looking probe for detection of tumor remnants and perisellar structures during microscopic transsphenoidal operations of sellar tumors. Adequate sellar enlargement by the tumor is a prerequisite to harbor the ultrasound probe intraoperatively. This represents a negative selection bias resulting in a shift to more difficult cases in our series.

Methods and materials

According to the current guidelines of the local ethic committee, we retrospectively evaluated data of patients transsphenoidally operated on sellar and parasellar tumors by the senior author between January 2009 and December 2013. Based on patient's files, operation reports, and available imaging, the following parameters have been evaluated: gender, date of birth, date of operation, age at operation, size of tumor, parasellar and suprasellar extension, and used intraoperative navigation method. According to surgical reports supra- and parasellar structures and tumor remnants detected with IOUS were documented as well as further resection based on IOUS results, estimated completeness of resection at the end of the operation based on IOUS, and limitation factors of IOUS. From the patient's files, any complications were recorded. Extent of resection based on MRI 3–6 months after the operation was documented. In case of hormone-secreting adenomas, remission or persistence of hypersecretion after operation was evaluated based on outpatient records of endocrinological tests.

Patients

Within 5 years, in our institution 286 microscopic transsphenoidal operations on sellar tumors were performed in 264 patients. IOUS for resection control had been used in 146 operations (138 patients), given that the sella was enlarged enough to harbor the probe's head after intrasellar tumor resection. Of these, complete data including follow-up were available in 113 operations on 107 patients. Fifty-eight of those operations were performed on male patients (51%) and 55 on female patients (49%), mean age 53 years, range 14 to 81 years. One hundred and ten operations were performed for pituitary adenomas and three operations for other pathologies (one of each Rathke's cleft cyst, craniopharyngioma, and xanthogranuloma). From the 110 operations on pituitary adenomas, 69 operations were performed on non-secreting and 41 on secreting adenomas: GH $N = 23$, ACTH $N = 8$ (including one case with Nelson's syndrome), PRL $N = 5$, TSH $N = 5$. Remission in acromegaly was defined by normal postoperative IGF-1 3 months after surgery, in Cushing's disease by subnormal postoperative serum cortisol, in prolactinomas by normal or subnormal postoperative PRL, and in secondary hyperthyroidism by normalized TSH and thyroid hormones. One hundred and three operations were done on macroadenomas and seven operations on microadenomas ($N = 1$) or small rests of former macroadenomas ($N = 6$), respectively. The maximal diameter was between 3 and 85 mm (mean diameter 26.6 mm). Out of the 110 operations on pituitary adenomas, 29 operations were performed on Knosp °0 tumors (26%), 15 operations on Knosp °I tumors (14%), 29 operations on Knosp °II tumors (26%), 24 operations on

Knosp °III tumors (22%), and 13 operations on Knosp °IV tumors (12%). Thirty-one (27%) operations were performed on patients previously operated on sellar tumors. The follow-up time was 3 to 49 months (mean 17.1 months). Table 1 shows the perisellar extension of pituitary adenomas according to Knosp grade.

Equipment and intraoperative use of ultrasound

All operations included in the current study were performed by one surgeon in modified Luedecke-Hardy technique using specula, instruments including mirrors to provide a panorama view also of the lateral areas of the surgical field, a combined suction/irrigation system (Link company, Norderstedt, Germany), an operation microscope (OPMI Pentero, Zeiss company, Oberkochen, Germany), and neuronavigation (Kolibri, Brainlab, Feldkirchen, Germany).

The applied ultrasound device was Aloka SSD 3500 (Aloka-Hitachi, Wiesbaden, Germany). The ultrasound probe used was a sterilizable linear field, side looking probe (UST-533 probe, Aloka-Hitachi) with head's diameters of $17.6 \times 6.9 \times 9.4$ mm, working with B-mode frequency between 4 and 13 MHz and flow mode frequency of 6 MHz (Fig. 1a). The scan width is 10 mm. The depth is adjustable up to 20 mm. The ultrasound probe is sterilizable by gas sterilization or plasma sterilization.

After completion of intrasellar tumor resection (either the surgeon supposed total tumor resection or suspected tumor remnants which he would not resect without intraoperative imaging), the ultrasound probe was placed into the fluid-filled sella, with gentle contact to its borders, and then rotated clockwise to gain view of the perisellar space (Fig. 1c–p). We propose the terms "direct contact" mode or "intracavitary" mode for this kind of intraoperative ultrasound imaging. If needed, the procedure was repeated several times after any further resection of tumor remnants. An illustrative case is given in Fig. 1a–r. The only case of a microadenoma was an ectopic adenoma in the cavernous sinus. Here the surgeon had to investigate the anterior parasellar space with the probe's head located in the sphenoid sinus in direct contact mode to the medial wall of the cavernous sinus.

Data analysis

The impact of IOUS on intraoperative decision making and further tumor resection has been elucidated. The extent of resection estimated intraoperatively at the end of the operation based on last IOUS was correlated to the MRI findings 3–6 months after the operation for all cases as well as to endocrinological tests in cases of hormone-secreting adenomas. The latter two parameters have been used as gold standard (if applicable). In case of discordance of data between late MRI and endocrinological state after operation of secreting pituitary adenomas, the latter were defined as assessment standard.

Using an internet provider (http://www.psychometria.de), sensitivity, specificity, positive predictive value, and negative predictive value of IOUS were determined. Based on the collected data, the resection rate stratified by preoperative Knosp grade was determined.
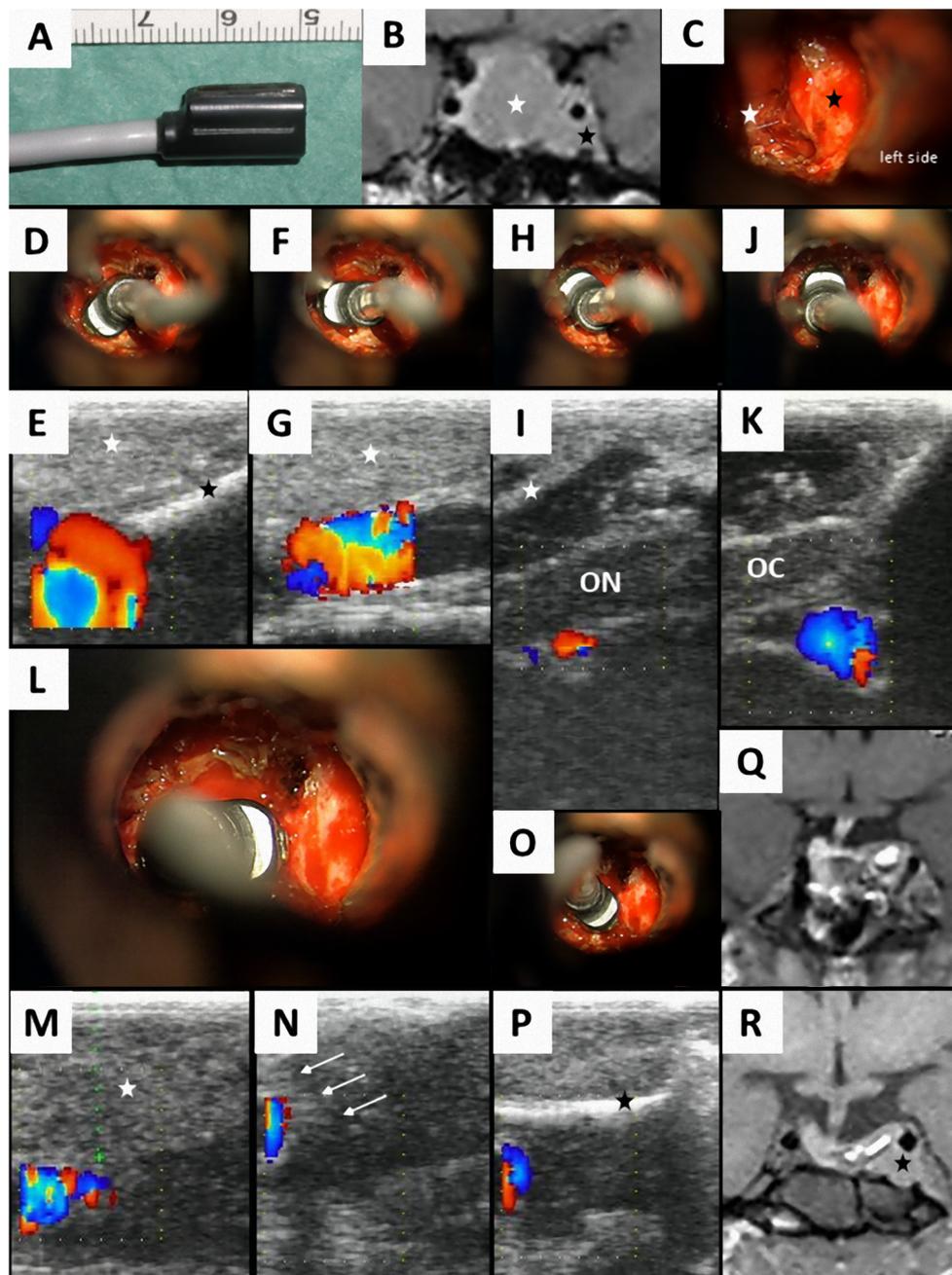
Results

Supra- and parasellar structures detected with IOUS

In the current study, in 112 out of 113 operations, the surgeon was able to detect all of the following structures by IOUS: internal carotid artery (ICA) in the cavernous sinus (CS), optic nerve (ON), optic chiasm (OC), and the A1 segment of the anterior cerebral artery (ACA) in the suprachiasmatic cistern. An exemplary case is given in Fig. 1 illustrating the standard directions of IOUS which were routinely used.

Extent of resection and remission rate

Complete resection of tumors stated by postoperative MRI after 3–6 months in this selected series was achieved in 75 of 113 operations (66%). However, in two of these patients, recurrent adenomas were detected during further follow-up. Table 2 gives a summary of the data on complete resection of pituitary adenomas ($N = 110$ operations) stated by MRI after 3

Table 1 Perisellar extension of pituitary adenomas in the series reported on correlated to Knosp grade obtained from preoperative MRI

Knosp grade	Suprasellar extension	Infrasellar extension	Right parasellar extension	Left parasellar extension
Knosp °0	21/29 (72%)	2/29 (7%)	0/29 (0%)	0/29 (0%)
Knosp °I	9/15 (60%)	0/15 (0%)	6/15 (40%)	10/15 (67%)
Knosp °II	20/29 (69%)	2/29 (7%)	20/29 (69%)	13/29 (45%)
Knosp °III	13/24 (54%)	2/24 (54%)	10/24 (42%)	17/24 (71%)
Knosp °IV	7/13 (54%)	0/13 (0%)	9/13 (69%)	9/13 (69%)

to 6 months postoperatively and stratified by preoperative Knosp grade.

Remission based on endocrinological tests 3–6 months after surgery was achieved in 18 of 41 operations of secreting pituitary adenomas (44%). In one patient, recurrent adenoma was detected during follow-up. Therefore, remission at the end of follow-up was achieved in 17 of 41 operations (41%). Table 3 depicts the data on remission rates correlated

to Knosp grade stated by endocrinological tests 3–6 months after surgery and at the end of follow-up.

Intraoperative consequences of IOUS

Further tumor resection was performed after detection of tumor remnants by IOUS in 65 out of 113 operations (58%), in the subgroup of secreting pituitary adenomas in 22 out of 41

Fig. 1 a Head of ultrasound probe used in this report (UST-533, Aloka-Hitachi, Wiesbaden, Germany). B-mode frequency 4–13 MHz, linear field, flow mode 6 MHz, diameter of probe 17.6 × 6.9 × 9.4 mm, adjustable depth up to 20 mm. **b–r** Illustrative case: **b** T1-weighted, gadolinium-enhanced coronary MRI of a 27-year-old female patient with acromegaly showing an intra- and suprasellar macroadenoma (white star) with infiltration of the left cavernous sinus (black star). Knosp Grade 3. **c** Intraoperative microscopic view after removal of the intrasellar and suprasellar tumor portion (white star) pointing towards the left cavernous sinus (black star). The surgeon is sitting against the patient. Therefore, the orientation in the images is vertically mirrored (right in the picture = left on the patient and vice versa). **d** Microscopic view of the introduced US probe which is scanning the lower right intra- and parasellar area. **e** The corresponding US image shows the decompressed pituitary (white star) close to the probe (top of any given US image), the ICA in the upper carotid canal posteriorly (left side of any US image) and the medial wall of the cavernous sinus (black star) more anteriorly (right side of any US image). **f** US probe pointing horizontally towards the right cavernous sinus identifying **g** the horizontal part of the right intracavernous ICA behind the pituitary gland (white star). Away from the probe (bottom in any given US image), the lateral wall of the right cavernous sinus is seen. **h** US probe pointing to the right upper perisellar area identifying **i** the diaphragm (white star), the right optic nerve (ON) longitudinally and above the latter (below in the image) the A1 segment of the right ACA. **j** In the midline, above the diaphragm **k** the optic chiasm (OC) with its anterior border and the anterior communicating artery are shown. **l** Aiming the US probe horizontally at the left cavernous sinus, **m** the intracaverous tumor remnant is visible (white star) with the left ICA behind it away from the probe. The tiny green dotted line represents the intraoperative measurement of the distance from the probe to the ICA, which was 4.8 mm in this case. **n** After safe opening of the cavernous sinus, most of the tumor could be resected without complications leaving a small visible tumor rest very close to the artery (white arrows). **o** Pointing to the lower left side, **p** the medial wall of the left cavernous sinus is identified (black star). **q** Coronary T1-weighted, gadolinium-enhanced MRI 1 day after surgery shows the pituitary gland preserved and decompressed, and the intracavitary filling material (fat). No tumor remnant detectable in early MRI. Partial remission was achieved endocrinologically, and gamma knife radiosurgery was applied to the tumor remnant in the left cavernous sinus **r** visible on MRI 3 months after surgery (black star). With ocreotide given in continually reduced dose acromegaly is controlled completely for more than 8 years. Visual and pituitary functions are intact

operations (54%). In 39 out of 65 operations, in which further resection after IOUS was performed, complete resection was achieved (60%) according to MRI after 3–6 months and/or endocrinological tests (in secreting adenomas). If no further

resection would have been performed at this intraoperative stage, complete resection would have been achieved in only 36 out of 113 operations. Thus, the rate of complete resection would have dropped from 66 to 32%.

Sensitivity and specificity of IOUS

According to MRI 3–6 months after the operation, the results of IOUS detecting tumor remnants were correctly positive in 21 operations, correctly negative in 68 operations, falsely positive in 7, and falsely negative in 16 operations. In one operation, the surgeon was not able to give a statement on suprasellar tumor remnants because of air in the suprasellar space. Therefore, sensitivity of IOUS was 0.568 and specificity was 0.907. The positive predictive value of IOUS was 0.750 and the negative predictive value was 0.810.

Perioperative morbidity and mortality

Intraoperative leakage of cerebrospinal fluid (CSF) occurred in 35 operations (31%). In 10 cases (8.8%), lumbar drainage was necessary. After two operations (1.8%), operative revision of CSF-leak was necessary. Diabetes insipidus occurred after 23 operations (20.4%). It was permanent after 3 operations (2.7%) and transient after 20 operations (17.7%). Transient SIADH occurred in two cases (1.8%). After two operations (1.8%), patients developed abducent nerve palsy, which was permanent in one case (0.9%). This was corrected later on by opthalmological intervention. One patient (0.9%) developed third nerve palsy, which resolved almost completely within months (minimal ptosis).

The following complications occurred two times each (1.8%): unilateral worsening of visus (one with bleeding into suprasellar tumor remnant), and postoperative nasal bleeding. One time each (0.9%) appeared: meningitis (after CSF-leak), mucocele, nasal synechia, sinusitis, nasal septum perforation, and transient psychosyndrome. Only after 56 operations, neither transient nor persistent minor or major complications were observed (50%). There was no mortality in this series.

Table 2 Confirmation of complete resection stated by postoperative MRI 3–6 months postoperatively correlated to preoperative Knosp grade. The table includes data of pituitary adenomas only

	Knosp 0	Knosp I	Knosp II	Knosp III	Knosp IV
Complete resection after 3–6 months	26/29 (90%)	9/15 (60%)	25/29 (86%)	12/24 (50%)	00/13 (0%)

Table 3 Postoperative endocrinological remission rate of pituitary hypersecretion syndromes reported on in this series ($N = 41$) correlated to preoperative Knosp grade of pituitary adenomas. Assessment by endocrinological tests 3–6 months after surgery and at the end of follow-up

	Knosp 0	Knosp I	Knosp II	Knosp III	Knosp IV
Remission after 3–6 months	6/6 (100%)	2/6 (33%)	6/8 (75%)	4/13 (31%)	0/8 (0%)
Remission at end of follow-up	6/6 (100%)	2/6 (33%)	5/8 (63%)	4/13 (31%)	0/8 (0%)

We believe that none of our complications were related to the use of IOUS.

Limitations of IOUS

The use of IOUS was limited by the following factors: air in the suprasellar space in 18 operations (16%), narrow sellar space in 5 operations (4%), scar tissue in 5 out of 31 secondary operations (16%), blood in 1 case (0.9%), and hemostyptic material in 1 case (0.9%). Despite limitations, the surgeon was able to detect all perisellar structures in all cases except one. In 85 operations (75%), no limitations occurred at all.

Discussion

The aim of the current study was to investigate the value of IOUS for resection control in transsphenoidal microsurgery. The findings of MRI 3 to 6 months after the operation were used as the evaluation standard for the amount of resection.

The decision to use the IOUS had been made intraoperatively, if allowed by anatomical conditions (such as size of the operation cavity in the sella). However, in most cases the surgeon was able to estimate preoperatively whether the use of IOUS would be suitable.

Ultrasound is known to be an experience- and user-dependent method. All operations in the current study have been performed by one surgeon; therefore, no variation of analysis is expected. However, better understanding with increasing experience seems to be probable.

The use of IOUS is simple and fast, and no specific operation instruments had to be applied. No complications caused by IOUS were observed.

Due to the retrospective design, data of 30 operations were incomplete and could not be included in the study. Despite a fixed timetable for follow-up investigations on the day of discharge, most patients came to first follow-up within 3 to 6 months after operation. Therefore, this time period was chosen, and other cases have been excluded for analysis.

In patients with secreting adenomas, no variation between evaluation of MRI and endocrinological tests has been found. However, since the evaluation of MRI has been performed in knowledge of endocrinological results, this may have caused a bias in radiological judgment.

The rate of complete tumor removal of 66% achieved in our series is comparable to results of other studies in the literature, whereas remission rate in secreting adenomas of 44% seems to be relatively low.

Mortini et al. presented a retrospective analysis of 1140 patients transsphenoidally operated on pituitary adenomas. The rate of radical removal was 64.8% in non-secreting and 66.1% in secreting adenomas. Especially in non-secreting adenomas, a clear relationship between size of tumor and radical tumor removal had been found (78.9% in microadenomas versus 55.5% in macroadenomas). The resection rate in adenomas with invasion of CS, defined as Knosp °III and °IV adenomas in this study, was only 7.4%. The time of follow-up was 3 to 6 months after operation as in our investigation. However, patients with recurrent adenomas previously operated upon had been excluded [28].

Similar results have been reported in another retrospective study of 491 patients operated on non-secreting adenomas. Complete resection, stated by MRI within 6 months after surgery, has been achieved in 63.6% of cases. Patients previously operated upon have been excluded as well [23]. In a series of 214 patients with acromegaly, complete resection has been achieved in 62.6% of cases, after secondary operations the rate of radicality was only 41% [15]. In a further study dealing with secreting pituitary adenomas, results of 86 patients operated on Cushing's disease showed complete resection after surgery in 60% of cases when preoperative MRI was negative, 83% in microadenomas, 94% when tumor was not invasive, and 40% of cases when the tumor infiltrated the CS [42].

In our cases, IOUS has been used if the tumor was large enough to create a sellar space which could harbor the probe's head after removal of the intrasellar tumor portion, many had a supra- and/or parasellar extension. Microadenomas with no extrasellar extension, which have a clearly better outcome according to the literature, had to be excluded for technical reasons. Only 7 of 110 operated pituitary adenomas in our series were smaller than 10 mm in diameter. Six of these had previously been operated on macroadenomas and had therefore a large sellar cavity making the use of IOUS possible. In the only one case with "true" microadenoma in this series, the TSH-secreting tumor was not previously operated but had a parasellar extension (Knosp °III). All other 103 cases were macroadenomas, with 34% of them being Knosp °III and °IV adenomas. These usually are considered to be infiltrating

the CS. Moreover, 27% of our cases have been previously operated upon, which also is correlated to a worse outcome. All this leads to a selection bias for difficult cases in the series reported here, allowing limited comparison with other studies. However, recurrent adenomas were found in only two of our cases after 16 and 32 months, respectively.

The time chosen for routine MRI evaluation in this study seems to be appropriate, with most studies cited having chosen the same time interval.

The selection bias for difficult cases in this series is also reflected in the relatively high number of perioperative complications reported here. Surgery for large tumors with suprasellar and parasellar extension is prone to produce inadvertant side effects, at least if radical tumor excision is aimed for. Other studies showed that the size of the tumor is one of the main factors which leads to complications [5]. The use of IOUS was introduced by us to improve resection rate particularly in difficult cases. This could partially explain complications of suprasellar resection in secondary cases on the one hand (e.g., CSF-leak, hemorrhage, and worsening of preexisting visual deficit) and of parasellar dissection on the other (e.g., disturbance of extraocular motor function). However, if needed, dissection close to and around the intracavernous ICA was performed without any injury of the ICA in this series.

We could not find an explanation for the fact that in our cohort the rate of complete resection was higher in Knosp °II adenomas than that achieved in Knosp °I adenomas. A recent study which evaluated invasion of CS using endoscopic technique supposed that other factors besides Knosp classification may predict invasion of CS. Especially in Knosp °III adenomas, the rate of invasion differed depending on whether the superior or inferior compartment of the CS was involved [27]. The low number of cases classified as Knosp ° I adenomas in this study may have contributed to the results, but the reason for this phenomenon remains obscure as in our series.

In 2010, Solheim et al. described the use of intracavitary IOUS with a prototype of a side looking probe starting utilization of this technique, like us, in 2008 [36]. In their first nine cases, they were able to visualize the perisellar anatomy very well in all cases. However, since this technique can be applied only after resection of the intrasellar tumor portion in a widened sella turcica, they developed a prototype of a straight looking probe for transsphenoidal use and reported on their experience with their first 24 cases [37]. With this technique, they were able to show the sellar and perisellar anatomy placing the probe into the water-filled sphenoid sinus. This resulted in convincing visualization especially of the suprasellar anatomy. The only (MRI-negative) microadenoma in Cushing's disease, however, was missed. Moreover, the parasellar space appeared of relatively low resolution, possibly due to bony artifacts. In these instances, the direct contact mode seems to be superior both for detection of (MRI-negative) microadenomas in approximately 2/3 of the cases with straight looking probes and visualization of parasellar tumor portions and the course of intracavernous ICA with side looking probes as reported by us [21, 33]. The latter also offers the crucial information to the surgeon how far exactly save dissection can be advanced in the lateral direction even above and below the horizontal part of the ICA. This may be due to the fact that the higher the frequency of the ultrasound probe, the better the resolution close to it.

Using IOUS, tumors remnants have been detected in 58% of our cases. This seems to be a high percentage for an experienced pituitary surgeon. However, the surgeon may tend to use IOUS early during the course of an operation to detect surrounding structures and to avoid their damage. Without using IOUS, the surgeon probably would not yet have stopped resection at this point. The same bias is also expected in other studies dealing with intraoperative imaging such as intraoperative MRI [2, 6, 11, 13, 30, 35, 44]. Especially resection at the lateral border of the sellar compartment close to the intracavernous ICA seems to be safe when done after identification of the vessel via IOUS. Therefore, the rate of complete tumor removal by using IOUS was improved. Despite the negative selection in our series mentioned above, we reach results of large series with otherwise unselected cases of primary operations only.

We use the microsurgical technique for transsphenoidal surgery with wide opening of the anterior wall of the sphenoid sinus including resection of the bony vomer. Therefore, we were able to introduce the rather bulky probe into the sphenoid sinus and also into the enlarged sella, which we routinely open widely as recommend by others [25]. For endoscopic technique, this may be a limitation for usage of this specific ultrasound probe. However, the supplier previously released a new side looking probe (Aloka UST-5311) with a diameter of less than 3 mm. This may on the one hand overcome the limitation of our technique to application to cases with enlarged sella only, and on the other hand make it useable by endoscopic surgeons as well. Further studies using both probes together should elucidate whether the quality of the images is comparable. Another limitation in our series was the restriction to a linear ultrasound field only. This has been solved with the next generation device of the hardware, which was introduced in our institution recently. It allows a trapezoidal view of the perisellar spaces improving the assessment of their anterior and posterior areas. A general limitation of ultrasound is air in the operating field. This explains some of our false negative results in cases with intraoperative CSF-leak. Blood and hemostyptic material may either blur the ultrasound images or resemble tumor tissue explaining some of our false positive results of IOUS. Others false positive results may be due to the fact that in a few cases the rather hypoechogenic tumor tissue was not delimitable from the pituitary gland itself. Moreover, comparing early and late postoperative MRI after

transsphenoidal operations, it has been reported that up to 40.5% of tumor remnants left behind may regress during the postoperative period [18]. In our experience, sensitivity of IOUS to detect tumor remnants far away from the probe was restricted. However, sensitivity of IOUS to identify resectable tumor remnants close to the probe seemed to be better, and frequently influenced intraoperative decision making. IOUS is safe and fast to perform, without time-consuming intervals during the operative progress, and without the need of specific instruments. Its commercial availability and the relatively low costs of the technique compared to intraoperative MRI may promote its further distribution and improvements to the devices.

Conclusion

Investigation of the perisellar compartments with IOUS during transsphenoidal surgery is simple, fast, and safe to perform. IOUS enables the surgeon to identify resectable tumor remnants intraoperatively, thus improving intraoperative decision making and the extent of resection.

Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speaker's bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patient-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Ethikkommission der Ärztekammer Westfalen-Lippe, Universität Muenster) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

For this type of study formal consent is not required.

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