**18**FDG-PET/CT computer-assisted biopsies for suspected persistent or recurrent malignant skull base disease.

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Running Title: PET-CT CAS for suspected persistent or recurrent malignant skull base disease.
Abstract

Background: FDG-PET/CT is increasingly used for the evaluation of regional or distant metastasis in head and neck oncology. However, positive PET findings lack specificity, which is especially challenging for localized disease at the skull base.

Methods: An optically tracked navigation system for multimodal image-guided biopsies was tested to evaluate PET-positive skull base lesions between 2009 and 2013.

Results: FDG-PET/CT navigated biopsies of patients with suspected persistence or recurrence of carcinoma (sinonasal, n=3; nasopharyngeal, n=1; adenocarcinoma, n=2; and carcinoma of unknown primary origin, n=1) have been safely performed. Histology confirmed local persistent or recurrent malignant disease (n=5), radio-osteonecrosis (n=1) and super-infection (n=1).

Conclusions: In the follow-up of tumor patients, FDG-PET/CT-navigated biopsies are a valid tool to evaluate PET-positive skull base lesions. This is an especially useful technique if functional anomalous areas in FDG-PET do not cause structural alterations in MRI/CT, and if endoscopic visualization is impossible because of post-treatment alterations.
Introduction

Following the general trend in head and neck oncology, $^{18}$F-Fluorodeoxyglucose-Positron Emission Tomography (FDG-PET) is used to a growing extent in primary staging or in the follow-up of skull base tumor patients. Moreover, FDG-PET and computed tomography (FDG-PET/CT) fusion imaging has very good sensitivity for the detection of recurrent regional or distant disease. PET/CT can detect abnormal metabolically functioning tissue areas even if this tissue appears structurally normal on MRI or CT. According to the most recently published recommendations, its role in the follow-up of skull base tumors is not yet fully defined. A positive predictive value (PPV) of 56% (95% CI: 0.31-0.77) and a negative predictive value (NPV) of 93% (95% CI: 0.81-0.98) have recently been reported for evaluation of local recurrence at the skull base. The high number of false-positive results in this study indicates a large problem for clinicians forced to perform potentially unnecessary invasive biopsies in between 22% and 50% of the patients. Moreover, the large range of the 95% confidence interval for the PPV reflects the histologically heterogeneous group of skull base tumors with a highly variable avidity for the FDG tracer.

Thus, incidental PET positive findings still need to be verified by precise biopsies to rule out competing diagnoses (e.g., osteomyelitis or fungal infections).

An accurate invasive evaluation of the skull base is clinically challenging because of the complex regional anatomy. Precise biopsies are technically demanding and can lead to devastating collateral damage due to the close proximity of vital neurovascular structures. Therefore, FDG-PET/CT-based computer-aided biopsy (FDG-PET/CT CAS) may be helpful because traditional endoscopic visualization may fail to locate the disease due to missing landmarks following surgery, scarring after radiochemotherapy or because of submucosal location of the recurrent disease.

According to our Medline Research, and in contrast to many reports on CT- and MR-based computer-assisted interventions, we did not find any systematic studies of bimodal FDG-PET/CT-based navigated biopsies in the skull base region. Until now, only for oral and oropharyngeal primaries, PET-
CT-based needle biopsies have been described in three patients by a German group of maxillofacial surgeons. Our study tested bimodal FDG-PET/CT fused computer-assisted biopsy for precise evaluation of FDG-PET-positive findings at the anterior skull base and its role as a new tool to confirm or rule out local tumor persistence or recurrence.

Materials and Methods

Between 1.1.2009 and 1.6.2013, we analyzed a subgroup of patients who had been referred to our outpatient clinic (tertiary referral clinic, Inselspital Bern) by the department of nuclear medicine because of small but highly suspicious FDG-PET/CT-positive findings at the skull base who underwent FDG-PET/CT CAS biopsy of the suspicious PET avid lesion. All patients had completed their first-line (multimodal) treatment. Because a standardized protocol for the use of FDG-PET/CT in the post-treatment follow-up of skull base patients did not exist, FDG-PET/CT restaging was performed at the discretion of the referring oncologist, radio-oncologist or ENT surgeon. Exclusion criteria were macroscopic gross disease with clearly identifiable pathologic changes in CT or MR and extensive local tissue alteration without the need for image-guided tissue sampling. Moreover, patients with multifocal disease with histological sampling performed distant to the skull base (i.e., regional cervical lymph nodes, lungs) were also excluded. All subjects were treated on an inpatient basis, and the intervention was performed under general anesthesia. Biopsy was performed using conventional endoscopic HD camera equipment and biopsy forceps (Karl Storz, Tuttlingen, Germany) and with the aid of the in-house developed multimodal navigation system described below. All of the patients gave their informed consent, and the study protocol has been reviewed and approved by the local ethics committee (Protocol Nr: R 10-07-13).

FDG PET/CT Imaging

FDG-PET/CT acquisitions were performed with an integrated PET/CT system (Biograph mCT 128™, Siemens Medical Solutions, Erlangen, Germany). All patients were kept on a
carbohydrate-free diet for at least 6 hours before the examination to assure a blood glucose level lower than 10 mmol/Lt prior to intravenous injection of 5–7 MBq FDG/kg body weight. Emission images of the trunk (neck to the pelvis) were obtained 90 minutes after injection (5–7 bed positions, 2 minutes per bed position) followed by dedicated high-resolution PET acquisition of the head and neck region (1 bed position, axial coverage 21.6 cm, 10 minutes per bed position). All PET images were reconstructed using an iterative time-of-flight (TOF) algorithm including point spread function correction (TrueX™). PET images of the trunk were reconstructed with a matrix size of 200x200, 5 mm Gauss filtering and a voxel size of 4 mm. High-resolution PET images of the head and neck region were reconstructed with a matrix size of 512x512, 2 mm Gauss filtering and a voxel size of 1.6 mm. PET images were coregistered with a low-dose CT scan (120 kV, 80 mAs, reconstructed slice thickness 2 mm) which was also used for attenuation correction. Following clinical routine, all PET/CT examinations were reviewed and reported by two board-certified nuclear medicine physicians with 6 and 11 years of experience in oncologic PET and PET/CT imaging. Visual interpretation of images was the preferred method in our institution, and similar to other institutional study protocols, standard uptake values (SUV) were not routinely measured\textsuperscript{8,9}.

FDG-PET/CT CAS System

A prototype of an optically tracked surgical navigation system integrated into a transportable setup (Figure 1A) was used as developed by the ARTORG Center at the University of Bern in collaboration with the Inselspital. The prototype was developed especially for the purpose of multimodal navigated biopsy\textsuperscript{10,11,12}. The system uses an optical tracking camera (NDI Vicra™, Northern Digital, Canada) to track reflective spheres mounted on standard surgical instruments, and the navigation software includes a standard pair point registration module. The navigation system and customized toolsets fulfill the fundamental requirements for medical devices according to the European Medical Device
Directive (93/42/EEC). All navigation adaptors and the tool calibration unit (Figure 1B, intra-operative setup) can be reprocessed and sterilized using standard hospital processing.

Hardware setup and clinical use

During the pre-operative phase, the co-registered FDG-PET and CT datasets were transferred to the navigation system. Pre-operative planning was performed using the automatically fused datasets (FDG-PET and CT) visualized on the three standard views (axial, coronal and sagittal) and volume rendered view (Figure 2). Preoperative planning consisted of defining the biopsy trajectory to ensure that there was no obstacle in between the entrance point and the target point. A special viewer showing the structures around the current trajectory was used to ensure an obstacle-free pathway (Figure 3 right). For patient to FDG-PET/CT registration, five bony landmarks (bilateral frontozygomatic sutures, nasion, bilateral interspaces between first upper premolar and incisors) were pre-operatively marked for intra-operative pair point matching (Figure 3 left).

During the intra-operative phase, the patient tracker was attached to the patient’s forehead and secured by an adjustable elastic cap. Instrument referencing was achieved with the use of a dynamic reference clamped onto the metal suction and biopsy forceps. The dynamic reference consists of a marker shield with retro-reflective spheres placed at well-defined positions. Sterile spheres were fixed to marker shields (Figure 2 right), and calibration of the instruments was performed. The calibration, i.e., detection of the position of the instrument relative to the dynamic reference, was dynamically calculated within a couple of seconds with the use of a calibration device.

The head of the patient was then registered with the image datasets by touching the tip of the calibrated forceps on five pre-defined landmarks on the patient. Pair-point matching between each landmark on the patient and its corresponding landmark defined in the image was subsequently performed by the system automatically. Final instrument guidance was achieved by joint display of the current position of the instrument on the patient’s anatomy on the virtual FDG-PET/CT display. A crosshair viewer aligned with the planned trajectory signaled the current position of the instrument...
by showing a cross representing the tip and a circle representing the shaft of the instrument. Four arrows on a millimeter grid indicated the distance from the center of the target area to the tip of the instrument (Figure 4 left). Additional viewers helped to highlight the area surrounding the instrument (Figure 4 right).

The time for the setup and the time for surgery were measured. Registration accuracy was clinically tested by landmarks deep in the skull base area; i.e., the center of the Eustachian tube (ET) orifice and the central apex level of the choana, both ipsilateral to the lesion. The target registration error (TRE) of the two landmarks was clinically estimated using the pointer tip diameter (1 mm). The navigated pointer tip was optimally centered on the virtual landmark on the CT image depicted by the navigation system. Keeping this position stable, we then estimated the deviation of the set pointer tip (corresponding to the virtual landmark) from the real position of the ET tube under endoscopic view.

Results

Suspicious FDG-PET positive lesions were localized in the previously treated primary tumor bed without other physical landmarks for proper localization; neither with endoscopy nor MR nor CT. The FDG-PET/CT exams were performed between three and 32 months after completion of initial multimodal therapy. The areas of high avid FDG uptake measured between 6 and 18 mm and were located 4 times in the roof of the anterior ethmoid, once in the posterior ethmoid and twice at the clivus.

The FDG-PET/CT CAS technique allowed reliable sampling or subtotal biopsy of the FDG-PET suspicious lesions for adequate histological workup. Neither fast frozen sectioning nor repetitive biopsy was needed to guarantee effective sampling. The results of the biopsies are depicted in table 1.
All biopsies for regional tumor persistence/recurrence were carried out under general anesthesia. Surgical intervention required 28 to 35 minutes to perform. The pre- and intra-operative times for the CAS setup were 15.8 minutes (range: 9.5 to 21) and 6.4 minutes (range 5.0 to 12.5), respectively. Clinically estimated TRE was in the range of 1 to 4 mm for the ET orifice. The TRE for the central apex level of the choana ranged from 1 to 3.5 mm. All interventions were well tolerated, with the occurrence of only minor complications (self-limiting mucosal bleeding). None of the patients suffered from major complications (e.g., CSF leak, visual impairment, major bleeding, meningitis). None of the patients needed nasal packing, and all patients could be dismissed on the next morning following the operation.

Two representative examples of FDG-PET/CT CAS of small PET-positive skull-base lesions

**Patient Nr. 3 with local recurrence of a poorly differentiated squamous cell carcinoma (SCC):**

At the age of 38, the male patient suddenly noticed a complete and persistent anosmia, which he and his physician related to a snowboarding accident one week before. One year later, the patient developed nasal obstruction and epistaxis, which led to the diagnosis of a locally advanced undifferentiated sinonasal carcinoma (cT4cN0cM0 according to the TNM classification). After induction chemotherapy, he received radical radiochemotherapy (cisplatin and total radiation dose of 72 Gy). After completing therapy, he showed no residual tumor, either in MRI or on endoscopy. Five months later, FDG-PET/CT revealed a 17-mm-large pathologic area at the upper region of the clivus. FDG-PET/CT navigated biopsy (Figure 4 and 5) proved local recurrence of the sinonasal carcinoma. Endoscopic salvage surgery was carried out. However, 16 months later, the patient developed a second intra-cerebral recurrence unrelated to the area of salvage surgery.

**Patient Nr. 7 with FDG-PET suspected 6-mm-large tumor recurrence in the clivus. The final cause was osteoradionecrosis following radiochemotherapy of a poorly differentiated nasopharyngeal carcinoma (cT3cN2acM0 according to the TNM classification):**
A 70-year-old female patient showed a focal hypermetabolic area on FDG-PET CT, paramedian left in the clivus, seven months after completion of radical radiochemotherapy (72 Gy, three times carboplatin) for cT3cN2acM0 undifferentiated nasopharyngeal carcinoma. Aside from a dry nose with nasal crusts, she was free of symptoms. Nasal endoscopy showed only post-radiogenic mucosal alterations without any other specific focal changes.

FDG-PET/CT CAS biopsy under general anesthesia was performed in the left clivus (Figure 6). Histology revealed a necrotizing inflammation and post-actinic endarteritis compatible with osteoradionecrosis. Twelve months later, the patient is still free from progression or loco-regional recurrence.

Discussion

Although the use of FDG-PET/CT is well established for head and neck SCC, only a few studies exist that have investigated its role in evaluating non-squamous carcinomas, and even fewer data are available on the rare subset of skull base tumors. Hence, the role of FDG-PET in the evaluation of skull base malignancies is still not fully defined.

The histologic grades of the majority of tumors in our series were undifferentiated neoplasias that showed high metabolic activity and avid pathologic FDG uptake; a characteristic feature of fast-growing tumors compared to other slowly growing tumors (e.g., adenoid cystic carcinoma, low grade esthesioneuroblastoma, mucinous tumors). The poorly differentiated adenocarcinoma and SCC in this study showed intense signals in FDG-PET/CT, which made possible the identification of lesions as small as 8 mm (and 6 mm in the case of focal osteomyelitis).

Only limited quantitative data are available for FDG-PET/CT examination of skull base malignancies in the literature. However, in other case series that have been published so far, poorly differentiated neoplasms had also been readily detected by FDG-PET uptake, e.g., malignant melanoma or SCC and adeno-carcinoma. Minimally invasive and precise biopsy is important for diagnosis and timely salvage treatment of skull base lesions. FDG-PET/CT is often reported to be the most sensitive
method for early detection of new primary tumors as well as for persistent or recurrent malignant skull base disease. Moreover, FDG-PET/CT has been shown to be more sensitive than CT or MRI. On the other hand, with the increased use of FDG-PET/CT, there has been a significant rise in the number of false positive PET findings, e.g., unspecific inflammation or osteoradionecrosis. In non-oncological cases, biopsy is also essential because purely medical or limited surgical treatment instead of radical surgery is often sufficient for cure.

Precise localization of the pathology with FDG-PET and CT fusion imaging is paramount and considered by some authors to be an additional valuable tool for diagnosis of early local recurrence. Based on FDG-PET/CT imaging, computer navigated biopsy provides the possibility of minimally invasive but reliable histological verification of suspected malignancy.

The additional time required for pre-operative image fusion and planning of the biopsy trajectory took an average of 16 minutes. Intra-operative time for registration of FDG-PET/CT with the actual patient’s head and calibration of the navigator pointer and biopsy forceps took the surgeon an average of 5 minutes. Total preparation time was comparable with CAS literature values for liver surgery, with 5 to 15 minutes but was longer than the 5.5 to 7.5 minutes needed for simple core needle biopsy. All biopsies were carried out under general anesthesia, and the actual surgical process required 20 to 35 minutes. None of the patients suffered from major complications. In all cases, reliable tissue samples were obtained with need for neither fast frozen section nor risky reposition of the biopsy. Target registration error (TRE) as clinically estimated was in the range of 1 to 4 mm. The TRE for the central point in the choanal apex ranged from 1 to 3.5 mm. These measurements of TRE are lower than the literature values of 4 to 10 mm for registration in soft tissue liver surgery and in a similar range to the TRE of 3.07 mm (1.2 SD) for soft tissue biopsies in porcine cadaver experiments.

In our series, in 5 out of 7 cases, the suspicious PET findings were true positive for local recurrent or persistent disease and false positive in 2 cases (once due to post-therapy osteoradionecrosis and
once due to unspecific inflammatory reaction). These findings are in accord with other case series. In a study by Gil et al., approximately one third of the FDG-PET positive findings were interpreted as false positive because of local inflammation or anomalous PET avidity in local flaps of complex skull base reconstructions (8 true positive compared to 4 false positive findings). More recent studies estimated for FDG-PET/CT a sensitivity versus a specificity of 100% and 50%\(^2\), 95% and 60%\(^2\) or 77% and 88%\(^5\). The lack of specificity of PET-positive findings is thought to cause 22% unnecessary invasive investigations of these skull base lesions\(^5\); a risky intervention for which FDG-PET findings have to be carefully weighed against discordant clinical findings\(^9\) and the individual wishes and needs of the patient.

In sum, FDG PET/CT has a high sensitivity for local recurrence and, based on these data, is supposed to be a good screening tool. However, its lack of specificity leads to a high number of false positive results requiring both safe and minimally invasive histologic workup. In our study, FDG PET/CT navigated biopsies have been a valid tool to evaluate incidentally PET-positive skull base lesions with high precision and minimal invasiveness in the follow-up of tumor patients. The technique was especially useful if functional anomalous areas in PET/CT did not correspond to structural alterations in MRI or CT, and if endoscopic visualization of the disease process was impossible because of scarring, crusts or postulated sub-mucosal tumor recurrence.

Conclusion

The novel application of FDG-PET/CT-guided biopsy using a prototype of a CAS navigation platform allows for safe and precise biopsy of subclinical minute lesions in the vicinity of the vital neurovascular structures of the skull base.

However, due to the small number of investigated patients and the rarity of the disease, it was methodologically not possible to show statistically the reduction of collateral damage and better tissue yield for FDG-PET/CAS biopsy compared to either conventional biopsy or watch and scan strategies. Nevertheless, it is our opinion that bimodal FDG-PET/CT computer-aided interventions are
a valuable tool to help the surgeon confronted with an increasing number of suspicious findings in FDG-PET/CT examinations and the problems related to this diagnostic Pandora’s Box.
Figures and Tables

Fig 1

Fig 2
<table>
<thead>
<tr>
<th>Patient Nr., sex, age</th>
<th>Histology</th>
<th>Initial TNM classification</th>
<th>Initial therapy</th>
<th>Time of restaging (mth)</th>
<th>Maximal diameter (mm) and Localization of PET-CT lesion</th>
<th>Biopsy results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, female, 61</td>
<td>Adeno Ca minor salivary gland (signet ring)</td>
<td>pt2cN2ccMo</td>
<td>S/RT</td>
<td>11 mth</td>
<td>7 mm, right L. cribrosa</td>
<td>Local recurrence</td>
</tr>
<tr>
<td>2, male, 60</td>
<td>Adeno Ca intestinal type villous</td>
<td>pt1cNocMo</td>
<td>S/RCT</td>
<td>32 mth</td>
<td>18 mm, right L. cribrosa</td>
<td>Local recurrence</td>
</tr>
<tr>
<td>3, male, 38</td>
<td>Poorly differentiated SCC</td>
<td>ct4cNocMo</td>
<td>RCT</td>
<td>5 mth</td>
<td>17 mm, right clivus</td>
<td>Local persistent disease</td>
</tr>
<tr>
<td>4, male, 55</td>
<td>Poorly differentiated SCC</td>
<td>ct4cNocMo</td>
<td>RCT</td>
<td>11 mth</td>
<td>16 mm anterior ethmoid</td>
<td>Local recurrence</td>
</tr>
<tr>
<td>5, female, 77</td>
<td>CUP of poorly differentiated SCC</td>
<td>ctXN2bcMo</td>
<td>S/RCT</td>
<td>3 mth</td>
<td>10 mm, anterior lateral ethmoid roof</td>
<td>Inflammation</td>
</tr>
<tr>
<td>6, male, 63</td>
<td>Poorly differentiated SCC</td>
<td>ct4N2bMo</td>
<td>S/RCT</td>
<td>13 mth</td>
<td>8 mm, posterior ethmoid roof</td>
<td>Local recurrence</td>
</tr>
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<td>7, female, 70</td>
<td>Poorly differentiated nasopharyngeal carcinoma (EBV positive)</td>
<td>ct4cN2c cMo</td>
<td>RCT</td>
<td>7 mth</td>
<td>6 mm right clivus</td>
<td>Osteoradionecrosis</td>
</tr>
</tbody>
</table>

Table 1: Histologic tumor types, initial staging with TNM classification (SCC: Squamous cell carcinoma, CUP: Carcinoma of unknown primary), initial therapy (S: Surgery, R: Radiotherapy, RCT: Radiochemotherapy) and with the size of PET-positive lesions and biopsy results.

<table>
<thead>
<tr>
<th>Patient Nr., sex, age</th>
<th>Preoperative set-up time (min)</th>
<th>Intraoperative set-up time (min)</th>
<th>Time for surgery (min)</th>
<th>TRE ET orifice (mm)</th>
<th>TRE choane (mm)</th>
<th>Biopsy results</th>
<th>Follow-up time after biopsy (mths)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, female, 61</td>
<td>18</td>
<td>5</td>
<td>33</td>
<td>1.5</td>
<td>1.5</td>
<td>Local recurrence</td>
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<tr>
<td>2, female, 60</td>
<td>15.5</td>
<td>6</td>
<td>28</td>
<td>1.5</td>
<td>1.5</td>
<td>Local recurrence</td>
<td>6</td>
</tr>
<tr>
<td>3, male, 38</td>
<td>20</td>
<td>12.5</td>
<td>35</td>
<td>4</td>
<td>2</td>
<td>Local persistent disease</td>
<td>25</td>
</tr>
<tr>
<td>4, male, 55</td>
<td>10</td>
<td>5</td>
<td>29</td>
<td>3.5</td>
<td>3.5</td>
<td>Local recurrence</td>
<td>15</td>
</tr>
<tr>
<td>5, female, 77</td>
<td>16</td>
<td>5.5</td>
<td>30</td>
<td>2.5</td>
<td>2.5</td>
<td>Inflammation</td>
<td>26</td>
</tr>
<tr>
<td>6, male, 63</td>
<td>21</td>
<td>6</td>
<td>32</td>
<td>1.5</td>
<td>1</td>
<td>Local persistence</td>
<td>13</td>
</tr>
<tr>
<td>7, female, 70</td>
<td>9.5</td>
<td>5</td>
<td>35</td>
<td>1</td>
<td>1.5</td>
<td>Osteoradionecrosis</td>
<td>24</td>
</tr>
</tbody>
</table>

Table 2: Technical details and results for the CAS system used (TRE: Target registration error, ET: Eustachian tube orifice).
Legends

Figure 1A: CAS workstation with camera, touch screens and computer unit. Fig 1B: Intra-operative setup of the CAS workstation featuring an upper monitor for planning and lower monitor for intra-operative CAS. A single person (surgeon on the left) can handle the whole registration and instrument calibration procedure under sterile conditions. Note: Reflection of instrument markers already mounted on a standard instrument (i.e., metal suction) as well as on the tool calibration unit used for optical tracking during surgery.

Figure 2: Planning mode for patient Nr 3: The combined FDG-PET automatically fused with low-dose CT allows precise localization of the PET-positive area with respect to the patient’s head.

Figure 3: Planning mode of the workstation for patient Nr 3 with FDG-PET-positive local recurrence of a sinonasal carcinoma localized at the bottom of the sphenoid sinus. The left part of the panel of the workstation (A) depicts four windows with a coronal, sagittal and axial views and with the 3-D volume reconstruction for the registration landmarks, defining at that moment point 0; i.e., left fronto-zygomatic suture. The right part of the panel (B) shows the axial plane including the planned trajectory (dotted line) for the biopsy instrument.

Figure 4: Combined FDG-PET and CT fused intra-operative navigation mode. The left part (A) shows the frontal section perpendicular to the planned biopsy trajectory. The instrument is not yet aligned (green cross for instrument tip and circle with cross for the instrument shaft). Four peripheral green arrows on the vertical and horizontal millimeter scale mark the distance to target in the z-axis (actually indicating a distance of 2.3 mm to the target center). The right side panel depicts the actual position of the instrument (green line) in relation to the desired final position (green dotted line) on the planned trajectory in both coronal (B) and sagittal (C) planes.
Figure 5: FDG-PET and CT fused intra-operative navigation mode with biopsy forceps in the target area. The left part of the panel (A) shows the frontal target view perpendicular to the planned biopsy trajectory. The biopsy instrument is now aligned on the x and z axes (yellow cross for the tip meets circle and cross for the shaft of the biopsy forceps). Green arrows on the horizontal and vertical millimeter scale fuse with the target center, indicating the correct position for the biopsy on the z-axis. Two panels on the right side depict the optimal position of the biopsy instrument on the planned trajectory with a green line in the coronal (B) and sagittal planes (C).

Figure 6:
Patient Nr 7 after radiochemotherapy of poorly differentiated nasopharyngeal carcinoma with a singular minute FDG avid area paramedian left on the clivus that was suspicious for local tumor recurrence. The left part of the panel (A) shows a frontal view of the target area perpendicular to the planned biopsy trajectory. The instrument (yellow cross for the tip and circle with cross for the shaft of the biopsy forceps) is perfectly aligned on the z-axis. Peripheral green arrows on the vertical and horizontal millimeter scale still show 1 mm distance to the optimal target center in the z-axis. The right part of the panel depicts the actual position of the biopsy instrument (green line) fitting to the desired final position on the trajectory in the coronal (B) and sagittal (C) planes.
References


