Journal of Cranio-Maxillo-Facial Surgery xxx (xxxx) xxx-xxx

Contents lists available at ScienceDirect

Journal of Cranio-Maxillo-Facial Surgery

journal homepage: www.elsevier.com

Diagnostic value of navigation-guided core needle biopsy in deep regions of the head and neck with focal FDG uptake on ^{18}F-FDG PET/CT

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ARTICLE INFO

Article history:
Received 9 July 2019
Accepted 14 February 2020
Available online xxx

Keywords:
Core needle biopsy
Navigation
Head and neck
PET/CT

ABSTRACT

Purpose

The aim of this study was to evaluate the feasibility and diagnostic accuracy of core needle biopsy (CNB) in patients with focal fluorodeoxyglucose (FDG) uptake on positron emission tomography/computed tomography (PET/CT) in deep regions of the head and neck, with the guidance of infrared navigation integrated with PET.

Materials and methods

Patients with suspected primary or recurrent malignancies of the head and neck on PET/CT, from June 2016 to December 2018, were included. Before CNB, the region of interest was delineated and the ideal needle entry points, target sites, and a number of trajectories were designed on iPlan CMF 3.0. CNB was performed with the guidance of infrared navigation integrated with PET, according to the pre-plan. Sensitivity and diagnostic accuracy were analyzed by comparing the biopsy results with the final diagnosis.

Results

Thirty-one consecutive patients were included. Among the 31 lesions, 18 were skull base, six were infratemporal fossa, and seven were maxillary region. The median values for SUVmax, SUVmean, and MTV were 6.09 (range: 1.43–24.67), 3.41 (range: 0.38–20.96), and 25.83 (range: 3.54–361.94) for the 31 lesions, respectively. Combined needle approaches were employed, including temporal (nine), subzygomatic (19), paramaxillary (11), and retromandibular (16) approaches. The depths of the 31 deep-region lesions, measured from the needle entry site on the skin to the target point, ranged from 1.33 cm to 7.82 cm (median 4.25 cm). There were three non-diagnostic lesions resulting from CNB, and these were all skull base. The diagnostic accuracy was 90.3%, while the sensitivity was 88%. According to the binary logistic regression for the final diagnosis, the only significant parameter was SUVmax.

Conclusion

With the guidance of navigation integrated with PET, CNB is a feasible and accurate diagnostic modality, which is also an alternative to open biopsy in patients with suspected primary or recurrent malignancies in deep regions of the head and neck on PET/CT.

1. Introduction

Accurate pretreatment diagnosis and evaluation during follow-up are necessary for monitoring and treating cancer patients. Histological diagnosis is considered the approach of choice when clinical examination and imaging techniques cannot differentiate malignancies and non-malignancies precisely. However, the traditional open biopsy of the head and neck increases the risk of tumor seeding, facial nerve injury, facial scarring, and fistula formation (Pfeiffer et al., 2012; Shah et al., 2016). Percutaneous biopsy has been one of the most cost-effective means of diagnosis for patients with suspected primary or recurrent malignancies. Fine-needle aspiration (FNA) — a diagnostic tool commonly used to obtain tissue specimens — was widely accepted as the first step in providing diagnostic information because of its cost-efficiency and relative speed, resulting in a sensitivity and specificity of 90–95% but yielding 10–15% non-diagnostic materials, despite its significant puncturing (Amedee et al., 2001). As an alternative approach, core needle biopsy (CNB) is thought to be superior to FNA in providing an accurate diagnosis, especially for nonsurgical patients such as those with lymphoid hyperplasia, as well as for subtyping and grading (Kraft et al., 2008). CNB provides an intermediate step between FNAC and open biopsy, and the tissue architecture is well preserved.

Positron emission tomography/computed tomography (PET/CT) using the glucose analog ^{18}F-fluorodeoxyglucose (^{18}F-FDG) is a non-invasive diagnostic tool that provides tomographic images and quantitative metabolic parameters (Szyszko et al., 2018). ^{18}F-FDG PET/CT is commonly utilized in the detection, staging, and prognosis of

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https://doi.org/10.1016/j.jcms.2020.02.009
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malignancies, in which FDG uptake correlates with the degree of local histological anaplasia — offering an accurate reflection of the tumor, with its anatomical heterogeneity. For patients with suspected primary or recurrent malignancies on PET/CT, with its high sensitivity and specificity, accurate histological diagnosis is then essential. Moreover, PET/CT-guided or assisted biopsy, as a diagnostic or prognostic assessment tool, is more accessible for surgeons in allowing them to recognize the region of interest (Feichtinger et al., 2010; Reinbacher et al., 2014).

Navigation platforms for percutaneous image-guided interventions, including image fusion and device tracking, enable surgeons to target challenging sites accurately with the potential of reducing risk during the procedure. The multimodality images coordinate with real-time displays to make sites in deep regions visible and accessible.

This study was performed to evaluate the feasibility and diagnostic accuracy of CNB in patients with focal FDG uptake on ^{18}F-FDG PET/CT in deep regions of the head and neck, with the guidance of infrared navigation integrated with PET.

2. Materials and methods

2.1. Patients characteristics

Patients with suspected primary or recurrent malignancies of the head and neck on PET/CT, from June 2016 to December 2018, were included. This study was approved by the ethics committee and was conducted under the guidance of international ethical standards (IRB number: PKUSSIRB-201942006). The final diagnosis was defined as the histological results of subsequent surgical treatment for the suspected malignancies or negative results with a follow-up of at least 2 years. Detailed information on the patients' characteristics are shown in Table 1.

2.2. Imaging protocols

Each enrolled patient underwent ^{18}F-FDG PET/CT scan before CNB. The patients were required to fast for at least 6 h before scanning to achieve a serum glucose level lower than 160 mg/dl. Then

Table 1
Patient characteristics.

Characteristics	Number (%)
Sex	
Male	15 (48%)
Female	16 (52%)
Age (years)	
Median	33
Range	2–65
Primary or suspected recurrence	
Primary tumor	16 (48%)
Suspected recurrence	15 (52%)
SUVmax	
Median	6.09
Range	1.43–24.67
SUVmean	
Median	3.41
Range	0.38–20.96
MTV (cm^3)	
Median	25.83
Range	3.54–361.94
TLG	
Median	99.65
Range	7.04–1281.27

MTV: metabolic tumor volume, SUVmax: maximum standardized uptake value, SUVmean: mean standardized uptake value, TLG: total lesion glycolysis.

^{18}F-FDG (96–330 MBq) was injected intravenously. The patients were scanned on a Philips Gemini TF16 PET/CT-scanner (Philips Medical Systems, Cleveland, OH, USA) with a 169 × 169 matrix and 4 mm slice thickness, along with low-dose CT images using a 512 × 512 matrix and 2 mm slice thickness for attenuation correction. In addition, contrast-enhanced CT (CECT) of the head and neck was performed on all patients using a GE Optima CT680 with a slice thickness of 0.75 mm.

For all patients, image registration between PET/CT and CECT datasets was performed using iPlan CMF 3.0 software (BrainLAB, Feldkirchen, Germany), allowing visualization of the exact anatomical localization of focal FDG uptake areas. The maximum standardized uptake value (SUVmax) threshold was adjusted according to the registered CECT. Then semiautomatic tumor segmentation was performed by two researchers. In line with the study protocol, features including metabolic tumor volume (MTV), SUVmax, and mean standardized uptake value (SUVmean) for the region of interest were calculated and recorded. Total lesion glycolysis (TLG) was defined as SUVmean multiplied by MTV.

2.3. Navigation pre-plan for lesions of deep regions

After registration between PET/CT and CECT datasets, two researchers delineated the region of interest and designed the ideal needle entry points, target sites, and a number of trajectories in consensus. Needle approaches from the needle entry point on the skin to the target, including temporal, subzygomatic, paramaxillary, and retromandibular directions, were designed to avoid bone, major blood vessels, and vital organs. Information on all trajectories and cervical vessels on the PET/CT and CECT datasets was imported to the navigation system (BrainLAB, Feldkirchen, Germany) for CNB. Bilateral cervical vessels were marked in conspicuous colors for identification during biopsy procedures.

2.4. Core needle biopsy

During the operation, patients were placed in a supine position under general anesthesia. Patients with lesions of deep regions of the head and neck require general anesthesia in order to reduce pain stimuli, maintain a stable position, and ensure an unobstructed airway. Navigation registration was performed before CNB. The navigation system included two parts: a computer platform on which needle trajectories on PET/CT and CECT datasets were displayed, and a localizer consisting of infrared-light optical cameras for detecting light from the digital reflective sphere. After importing data, the surgeons registered multiple points on the face to match the surface profile of the CT dataset.

After navigation registration, the patient's actual head position was correlated with the virtual position on the navigation system, and then the surgeon performed CNB according to the pre-plan. CNB was performed with a spring-loaded semiautomatic biopsy gun (Bard Magnum; Bard Inc., Covington, GA) with side-notch needles of 10 cm length (diameter 14 gauge). When the gun was triggered, an inner trocar with a sample , and simultaneously the outer cannula, would thrust forward and shear off a specimen with minimal crushing. Technical success was defined as an appropriate location of the needle tip for accessing the target lesions and sufficient specimens on visual inspection (Kim et al., 2015). The surgeons repeated this biopsy procedure to obtain sufficient specimens for histological examination. The number of samples depended on the suspected histological diagnosis of the tumor, the location of the lesion, and the quality of specimens obtained. Each needle path was repeated three times to obtain sufficient sample tissue. After the biopsy procedure, the puncture site on the skin was compressed manually for about 5 min to control bleeding. Patients were observed for bleeding, swelling, pain, and other complications after the operation. Sensitivity and diagnostic accuracy were analyzed by comparing the biopsy results with the final diagnosis.

2.5. Statistical analysis

A binary logistic regression analysis, using a backward conditional method, was performed for parameters including SUVmax, SUVmean, and MTV to predict the final diagnosis. The cut *p*-values were defined as 0.05 . Statistical analysis was carried out using SPSS 13.0 for Windows (SPSS Inc, Chicago, IL, USA).

3. Results

Thirty-one consecutive patients with suspected primary or recurrent deep-region malignancies on PET/CT were included in this study. Among the 31 lesions of suspected deep-region primary or recurrent malignancies on PET/CT, 18 were skull base, six were infratemporal fossa, and seven were maxillary region. Combined needle approaches were employed, including temporal (nine), subzygomatic (19), paramaxillary (11), and retromandibular (16), with navigation guidance (Figs. 1–4). The depths of the 31 lesions of deep regions, measured from the needle entry site on the skin to the target point, ranged from 1.33 cm to 7.82 cm (median, 4.25 cm). The medians and ranges of SUVmax, MTV, and TLG are shown in Table 1.

All the specimens were adequate for histological diagnosis. Twenty-five patients were diagnosed as malignancies and six were negative according to the final diagnosis. Adenoid cystic carcinoma was the most common type (9/25), followed by rhabdomyosarcoma (8/25), and squamous cell carcinoma (4/25). Four other types — mucoepidermoid carcinoma, fibroma, osteosarcoma, and primitive neuroectodermal tumor — each affected one patient. There were three non-diagnostic lesions according to CNB giving a diagnostic accuracy of 90.3% (28/31), while the sensitivity was 88% (22/25). The three non-diagnostic lesions were all skull base. According to the binary logistic regression for the final diagnosis, the only significant parameter was SUVmax and the odds ratio was 1.539 (95% confidence interval: 0.902–2.627).

The most common complication after CNB was bleeding, which could be controlled by local compression. Other potential complications, such as hematoma, pain, and cranial nerve injury, were not observed in any patient.

4. Discussion

^{18}F-FDG PET/CT shows high accuracy in the detection of malignancies, but its relatively poor spatial resolution limits its ability to delineate the extent of the tumor and the relationship of the tumor with the surrounding structures, which is of great importance for accurate T staging and surgical planning (Goerres et al., 2008). Also, false-positive results are prone to occur at sites adjacent to areas of high physiological FDG activity and with tumors tending to harbor inflammatory processes. In this study, the results showed that the final diagnosis was inclined to be malignant for lesions with higher SUVmax values. Most of the limitations of PET for T classification can be mitigated if simultaneous diagnostic CECT is performed for attenuation correction and to define target volumes (Moule et al., 2010). Moreover, the bone and major blood vessels in CECT can be avoided, especially for lesions of deep regions of the head and neck.

Biopsies are necessary for patients with suspected primary or recurrent malignancies on PET/CT or other radiological modalities. CNB, as a simple, minimally invasive, and accurate method for the diagnosis of head and neck lesions, such as cervical lymphadenopathy (Lin et al., 2017; Han et al., 2018) and suprahyoid lesions (Wu et al., 2013), can be applied with the guidance of ultrasound and com-

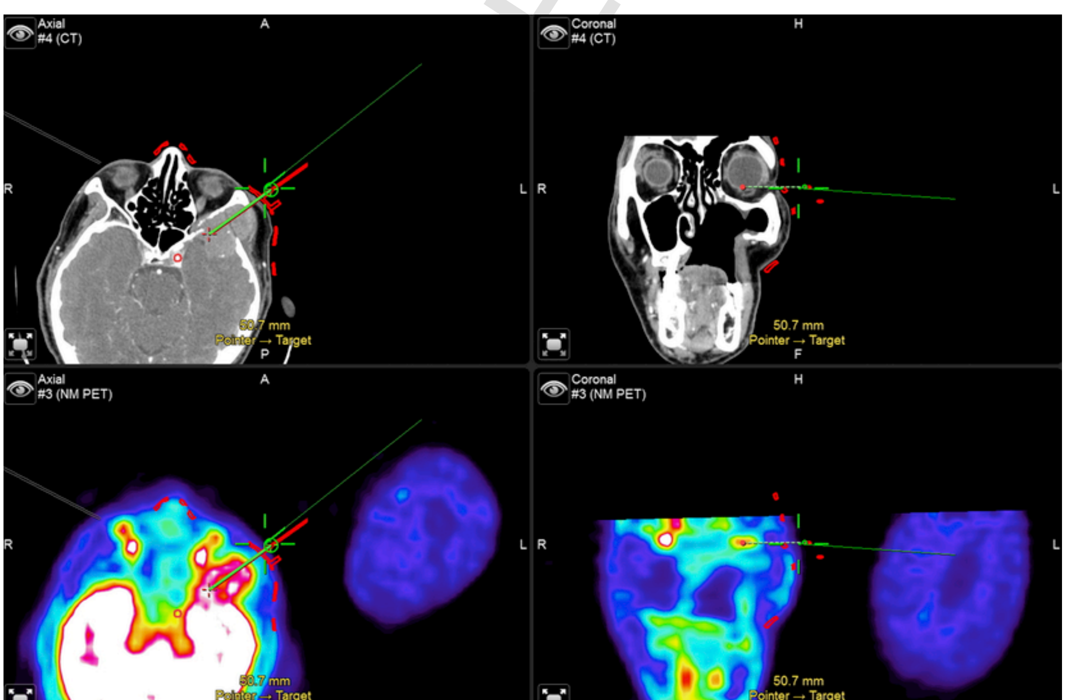

Fig. 1. A 53-year-old male with suspected recurrent adenoid cystic carcinoma undergoing CNB via a temporal approach with navigation guidance.

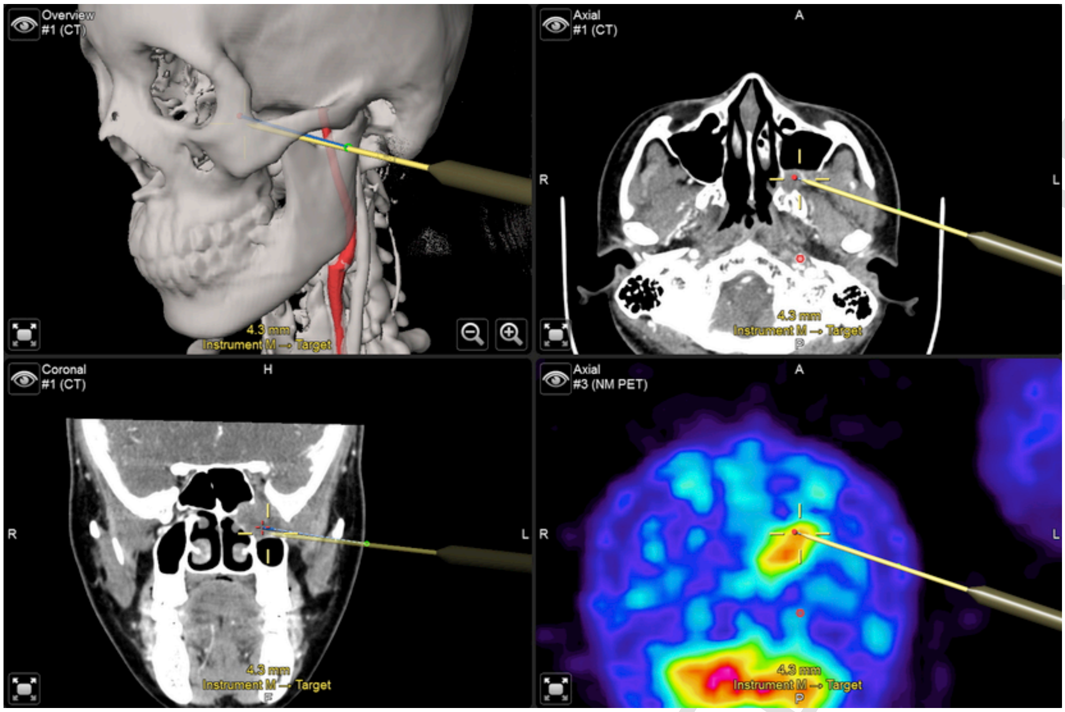

Fig. 2. An 18-year-old female with suspected recurrent rhabdomyosarcoma undergoing CNB via a subzygomatic approach with navigation guidance.

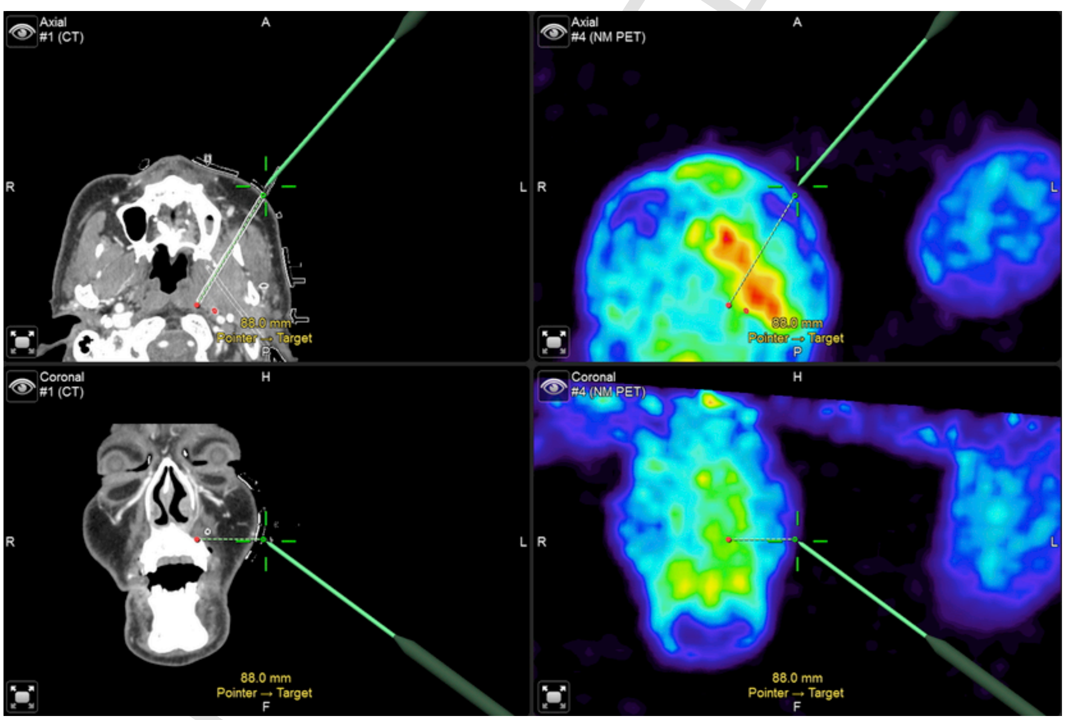

Fig. 3. A 56-year-old male with suspected primary adenoid cystic carcinoma undergoing CNB via a paramaxillary approach with navigation guidance.

puted tomography. Ultrasound guidance is a cost-effective method for reducing risks associated with CNB, but it is limited in its application for deep regions because of distal acoustic shadowing (Pfeiffer et al., 2007). Publications evaluating CNB in the head and neck field have been reported mainly by interventional radiologists (Novoa et al., 2012), where vital structures around the lesions were scrutinized to obtain an optimal needle pathway that prevented neurovascular injury. Studies concerning the biopsy of lesions of deep regions, such as skull base, are limited, and the guiding techniques used have been mainly CT-based (Abrahams, 1998; Connor et al., 2008; Wu et al., 2013). CT-guidance of higher spatial resolution is more suitable for the head and neck because of its reduced image degradation

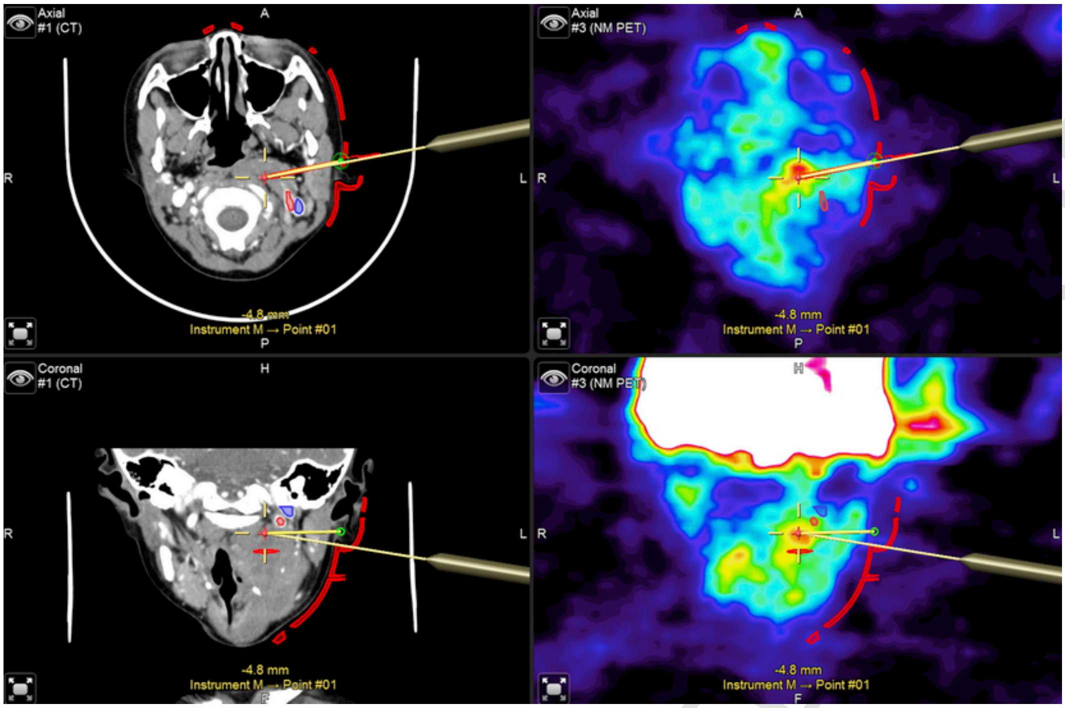

Fig. 4. A 6-year-old female with suspected recurrent rhabdomyosarcoma undergoing CNB via a retromandibular approach with navigation guidance in order to avoid the carotid sheath.

from intervening osseous-to-air structures (Sherman et al., 2004). CT-guided FNA is 86–88% accurate (DelGaudio et al., 2000; Sherman et al., 2004), but the conventional CT-guided technique lacks real-time feedback during the biopsy procedure. Real-time CT-fluoroscopy guidance (Chan et al., 2010; Grand et al., 2011) or cone-beam CT guidance (Abi-Jaoudeh et al., 2012; Kickuth et al., 2015) remains scarce, with CNB for deep regions presenting a challenge.

The three non-diagnostic lesions in this study were all skull base, which reflected the difficulty and uncertainty of biopsy of deep regions of the head and neck. With vital organs or bony structures located in the biopsy path, the routine angled gantry approach struggles to access the target. Researchers have employed a range of approaches, including temporal, subzygomatic, paramaxillary, and retromandibular (Wu et al., 2013) for nonpalpable, deep-located lesions of the head and neck, including the infratemporal fossa and skull base (Sherman et al., 2004). Subzygomatic and paramaxillary approaches have been used in the masticatory, parapharyngeal, and retropharyngeal spaces (Gupta et al., 2007). For infratemporal tumors, the needle avoids bony structures (zygoma, temporal bone, and maxilla) to reach its targets. Subzygomatic and temporal approaches, with navigation guidance, are the main paths used to prevent contact with the maxillary artery, pterygoid venous plexus, vital nerves, and vessels of parapharyngeal space. The retromandibular approach is used for the lateral skull base, with the direction and depth of needle paths guided by navigation to avoid the internal carotid artery and jugular foramen. The paramaxillary approach with pre-planning and navigation assistance allows bypassing of the medial canthal and paranasal areas, ensuring that the target points are not located in cavities such as paranasal sinus or maxillary sinus, and avoiding injury to the lacrimal duct and infraorbital nerve.

The potential for tumor seeding as a result of CNB varies greatly depending on tumor type and anatomic site (Shah et al., 2016). Novoa et al. performed a systematic review and meta-analysis of raw data extracted from 16 studies, involving 1291 lesions, including those affecting salivary glands and lymph nodes. The results showed CNB to have higher accuracy (96% vs 93%) and specificity (99% vs 96%) than FNA, and found no cases of tumor seeding in 438 lesions, with 7 years of follow-up (Novoa et al., 2012). Sampling errors can occur when tumors are insidious or ambiguous. These can be prevented by taking samples from multiple sites, avoiding the necrotic and inflammatory areas, and targeting the most aggressive parts of lesions. Usually, non-representative diagnoses occur if the sample shows evidence of inflammatory reactions or fragments of fibrosis, while non-diagnostic samples present only scant tumor tissue (Ha et al., 2014; Kickuth et al., 2015).

Navigation guidance based on PET/CT has been used for surgical planning of head and neck tumor resection and reconstruction, as well as for intraoperative control of resection margins in advanced head and neck cancer (Feichtinger et al., 2010; Reinbacher et al., 2014; Zrnc et al., 2018). Navigation in the field of maxillofacial surgery has been applied to trauma, orthognathic surgery, tumor ablation with reconstruction, skull-base surgery, and foreign body removal (Azarmehr et al., 2017). To optimize the efficacy of interventional modalities and decrease dependence upon operator experience, navigation methods including image fusion and device tracking have emerged, enabling surgeons to reduce the risks associated with biopsy (Rajagopal et al., 2016). Navigation allows real-time referencing, which enables the tracking of needles, with rapid image processing technology displaying multiplanar and fused images that improve lesion targeting (Wood et al., 2010). Moreover, CNB with navigation guidance can improve accuracy and reduce needle distance to the target while minimizing off-path errors (Appelbaum et al., 2011; Krücker et al., 2011; Venkatesan et al., 2011; Choi et al., 2012). Establishing paths that avoid bone, major blood vessels, and vital organs in the pre-planning stage also reduces the risk of vital structure injury and hemorrhage. CT-guided and US-guided biopsy procedures are the usual modalities, while PET integrated with CT/US-guidance has been practiced in abdominal and thoracic fields (Venkatesan et al., 2011; Paparo et al., 2014), as well as head and neck (Pfeiffer et al., 2009). As our study has shown, by integrating navigation guidance with PET, lesions in deep regions of the head and neck become more clearly visible and accessible, making it easier for surgeons to perform CNB.

The relatively small sample size was one of the limitations of this study. Moreover, accuracy assessment was not applied. Deformation of soft tissue and the needle may have affected entry points and the subsequent paths taken. However, our study shows that, for difficult cases, intraoperative CT-guidance combined with infrared navigation can be used to confirm the target point.

5. Conclusion

With navigation guidance integrated with PET, CNB is a feasible and accurate diagnostic modality, and is also an alternative to open biopsy in patients with suspected primary or recurrent malignancies in deep regions of the head and neck according to PET/CT.

Declaration of Competing Interest

The authors declare no conflicts of interest.

Funding

This work was supported by the Program for New Clinical Techniques and Therapies of Peking University School and Hospital of Stomatology [PKUSSNCT-13A08].

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