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·临床研究·

磁共振成像评估舌鳞状细胞癌浸润深度的准确性分析

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【摘要】 目的 以光镜下病理切片为参照，分析磁共振成像(magnetic resonance imaging，MRI)测量的舌鳞状细胞癌浸润深度的准确性，为临床提供参考。**方法** 选取2018年1月至2020年9月就诊于山西医科大学第一医院口腔科和中南大学湘雅口腔医院的73例舌鳞状细胞癌患者，术前均行MRI评估舌鳞状细胞癌浸润深度，术中冰冻病理切片再次测量舌鳞状细胞癌浸润深度。**结果** T1加权成像测量的舌鳞状细胞癌浸润深度较病理结果平均高估1.11 mm (95%*CI* = 0.51 ~ 1.70，t = 3.72，P < 0.001)，相关系数r为0.95；T2加权像平均高估2.17 mm (95%*CI* = 1.32 ~ 3.02，t = 5.10，P < 0.001)，相关系数r为0.92。Bland-Altman图显示T1、T2加权像与病理测量的浸润深度一致性佳。**结论** MRI测量的舌鳞状细胞癌浸润深度较为准确，与病理测量结果相比有平均1 ~ 2 mm的高估，其中T1加权像优于T2加权像。

【关键词】 鳞状细胞癌；舌鳞状细胞癌；口腔鳞状细胞癌；口腔癌；舌肿瘤；浸润深度；磁共振成像；病理检查
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Accuracy analysis of MRI in the depth of invasion assessment of tongue squamous cell carcinoma

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【Abstract】 Objective To analyze the accuracy of the infiltrating depth of tongue squamous cell carcinoma measured by magnetic resonance imaging (MRI) using pathological sections under a light microscope to provide a clinical reference. **Methods** Seventy-three patients with tongue squamous cell carcinoma who visited the Department of Stomatology of the First Hospital of Shanxi Medical University and Xiangya Stomatological Hospital from January 2018 to September 2020 were selected. Preoperative MRI was performed to evaluate the infiltration depth of tongue squamous cell carcinoma, and intraoperative frozen pathological sections were used to confirm the infiltration depth of tongue squamous cell carcinoma measurement. **Results** The infiltration depth of tongue squamous cell carcinoma measured by T1-weighted imaging was 1.11 mm (95% *CI* = 0.51−1.70; t = 3.72; P < 0.001), and the correlation coefficient r was 0.95. The T2-weighted average overestimation was 2.17 mm (95% *CI* = 1.32-3.02; t = 5.10; P < 0.001), and the correlation coefficient was 0.92. The Bland-Altman plot showed good consistency between T1- and T2-weighted images and pathologic measurements. **Conclusion** The infiltration depth of tongue squamous cell carcinoma measured by MRI is more accurate, with an average overestimation of 1−2 mm compared with pathological measurements, and T1-weighted images are better than T2-weighted images.

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【Key words】 squamous cell carcinoma; tongue squamous cell carcinoma; oral squamous cell carcinoma; oral cancer; tongue neoplasms; depth of invasion; magnetic resonance imaging; pathological examination
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舌组织缺乏解剖屏障，富含血管和淋巴组织，因此舌鳞状细胞癌具有较强的侵袭性和颈淋巴转移倾向。据报道，舌鳞状细胞癌颈淋巴转移率为31%～58%，早期舌鳞状细胞癌常发生隐匿性颈淋巴转移[1-3]。大量研究证实肿瘤厚度是预测舌鳞状细胞癌颈淋巴转移的重要的独立因素[4-6]。据文献报道，大于4 mm的浸润深度可作为临床颈淋巴结阴性的舌鳞状细胞癌患者行预防性颈淋巴清扫的参考标志[7]。浸润深度的测量定义最初由Jung等[8]提出，随后由美国癌症联合委员会（American Joint Committee on Cancer，AJCC）完善并新增入第八版口腔癌TNM分期中T分类指标，其最新定义是指肿瘤与其两侧最邻近的正常黏膜基底膜交点的连线至肿瘤浸润最深处的垂直距离，较肿瘤厚度能更好地反映肿瘤靠近血管和淋巴管的程度。术前对浸润深度的评估不仅有助于舌鳞状细胞癌的临床分期，也有助于颈清选择和手术切缘的确定。临床浸润深度的评估有触诊以及磁共振成像（magnetic resonance imaging，MRI）、电子计算机断层扫描（computed tomography，CT）等影像检查，其中MRI是理想的软组织检查方法，较触诊具有可重复性。然而目前对于具体的MRI测量序列仍有争议，因此本项研究主要比较了MRI中T1、T2加权序列测量的舌鳞状细胞癌浸润深度的准确性，以期为舌鳞状细胞癌术前TNM分期、手术切缘的设计和颈淋巴转移的预测提供影像参考。

1　资料和方法

1.1　研究对象

本研究为前瞻性研究，选取2018年1月至2020年9月在山西医科大学第一医院和中南大学湘雅口腔医院就诊的舌鳞状细胞癌患者，其中包含原发舌部，波及口咽、口底等邻近软组织的舌鳞状细胞癌病人。纳入标准：经病理证实为舌鳞状细胞癌的患者；术前均未行放、化疗；患者无全麻及手术禁忌症；既往无舌肿瘤史。排除标准：对MRI检查有禁忌症；口腔内有金属义齿或大面积牙内金属充填材料不愿去除的患者；未接受手术治疗或切缘阳性者。

共纳入73例患者，其中男性43例，女性30例，年龄32～83岁，平均年龄（58 ± 12）岁。依据第七版口腔癌TNM分期，T1分类舌鳞状细胞癌患者10例（14%），T2分类舌鳞状细胞癌患者23例（31%），T3分类舌鳞状细胞癌患者19例（26%），T4分类舌鳞状细胞癌患者21例（29%）。以第八版口腔癌TNM分期中的T分类为标准，pT1（浸润深度 ≤ 5 mm，最大径 ≤ 2 cm）患者5例（7%），pT2（5 mm < 浸润深度 ≤ 10 mm，最大径≤4 cm或浸润深度≤5 mm，2 cm < 最大径 ≤ 4 cm）患者18例（24%），pT3（浸润深度 > 4 mm或最大径 > 4 cm）患者29例（40%），pT4（肿瘤浸润邻近的其他组织，但不包括颏舌肌、舌骨、腭舌肌和茎突）患者21例（29%）。

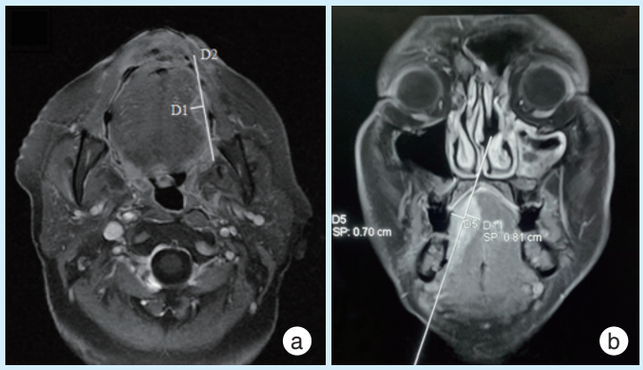
1.2　研究方法

纳入的患者于手术前10 d内完成MRI检查，检查期间患者呈平卧位，头后仰且位于正中位，不偏斜、不吞咽和不说话。

使用的MRI设备均为3-Tesla（T）场强（美国GE，Signa HDxt；荷兰Philips，Achieva 3.0T TX）和八通道正交头颈部线圈，获得轴向和冠状自旋回波T2加权成像（TR/TE，3 000-4 000/80 ms）和横断位和冠状T1加权成像（TR/RE，500-600/15 ms）。均采用薄层扫描，层厚1～1.25 mm，层距1 mm；视野（FOV）180 mm或220 mm。经静脉注射对比剂Gd-DTPA（0.1 mmol/kg），分别在T1和T2加权序列上行横断面、矢状面和冠状面扫描。

1.2.1　影像测量　影像图片以DICOM格式导入syngo.via软件后，影像科评估者分别测量核磁T1、T2加权成像中肿瘤的最大浸润深度，测量方法为：连接肿瘤与其最邻近的正常黏膜交点的连线，测量该连线至肿瘤浸润最深处的垂直距离（图1）。对于MRI上无肿瘤显示的病例浸润深度记为0 mm。

1.2.2　病理测量　将手术标本沿冠状位或横断位间隔3～5 mm切开或正中切开，随后冰冻切片机中连续切片选取肿瘤浸润最深部分制作病理切

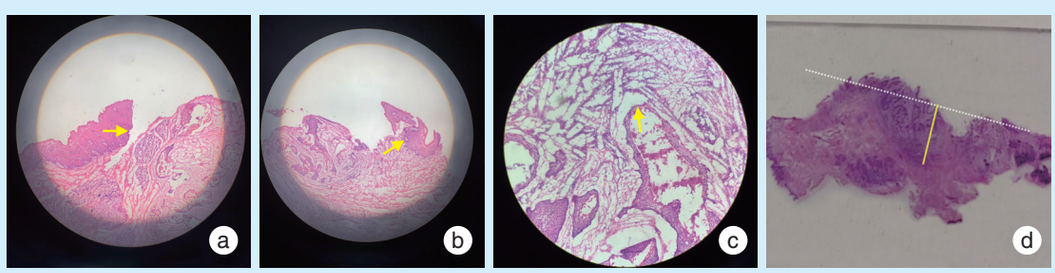


a: coronal position measurement; and the normal mucosal wiring of the tumor closest to it was identified, and the distance between the line and deepest depth is the tumor depth of invasion; b: the transverse location measurement schematic diagram, and the measurement method is the same as in that figure la

Figure 1　Invasive depth of tongue squamous cell carcinoma measured by MRI

图1　MRI测量的舌鳞状细胞癌浸润深度

片。采用75 mm × 60 mm规格的载玻片(江苏南通,求精实验耗材商城),经苏木精、伊红(HE)染色后在显微镜下测量。因标本黏膜表层常不完整,因此测量时以黏膜基底膜为基线,测量方法如图2所示:显微镜下确定肿瘤与其两侧最邻近的正常黏膜基底膜的交界点以及肿瘤细胞的浸润最深点并用记号笔在载玻片下标记,随后连接的标记点并测量肿瘤的最大浸润深度。



a-b: the yellow arrows represent the intersection point of the tumor and the closest basal membrane of normal mucosa on both sides under the microscope (HE, ×40); c: the yellow arrows represent the deepest point of tumor cell infiltration (HE, ×200); d: the yellow lines represent the depth of tongue squamous cell carcinoma infiltration (HE)

Figure 2　Schematic diagram measuring the pathological infiltration depth of tongue squamous cell carcinoma

图2　舌鳞状细胞癌病理浸润深度的测量示意图

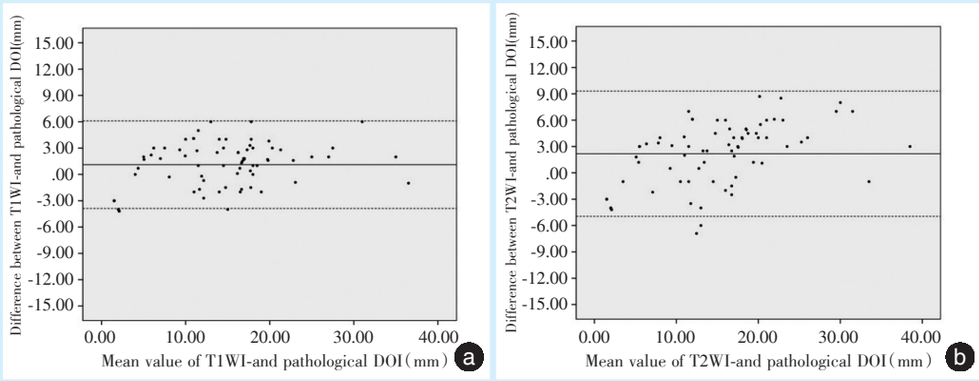
1.3　统计学处理

采用统计软件SPSS 22.0分析数据,K-S检验分析测量的数据是否符合正态分布,Levene检验方差齐性,若方差齐则采用配对样本t检验计算MRI与病理测量的浸润深度差异及95%可信区间(confidence interval, CI)。采用Bland-Altman散点图中95%一致性界限(95% limits of agreement, 95% LoA)展示MRI各加权序列与病理测量结果的一致性。采用Pearson相关分析MRI各序列测量的舌鳞状细胞癌浸润深度与病理测量结果的相关性。

2　结　果

73例患者中,镜下病理切片测量的浸润深度为(14 ± 7.1)mm,T1加权成像测量的浸润深度为(15.1 ± 7.9)mm,T2加权像测量的浸润深度平均为(16.2 ± 8.9)mm。配对样本t检验表明T1加权成像测量的舌鳞状细胞癌浸润深度较病理平均高估1.11 mm(95%CI = 0.51 ~ 1.70, t = 3.72, P < 0.001);T2加权成像测量的浸润深度平均高估2.17 mm(95%CI = 1.32 ~ 3.02, t = 5.10, P < 0.001)。

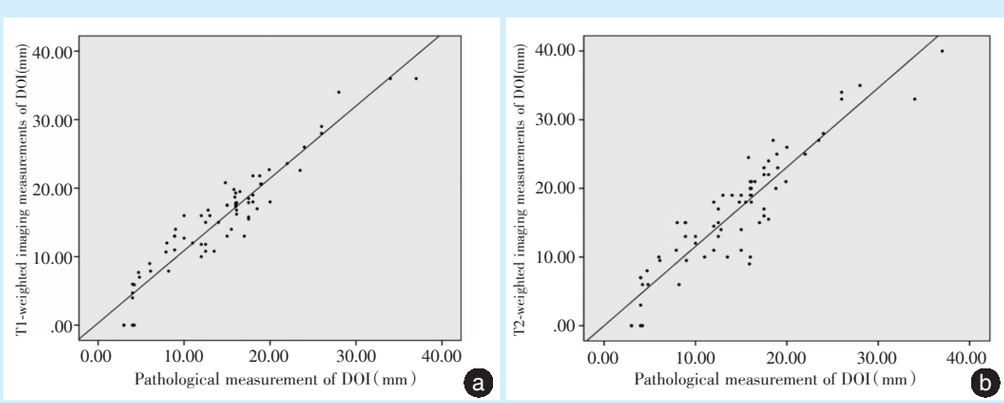
Bland-Altman散点图显示了MRI中T1、T2加权成像与病理测量的舌鳞状细胞癌浸润深度的一致性(图3);核磁T1加权像与病理测量的浸润深度相关系数r = 0.95, P < 0.001;T2加权成像与病理测量的浸润深度相关系数r = 0.92, P < 0.001(图4)。



The solid line is the average difference, and the dotted line is the 95%LoA of the difference. The mean difference in the invasion depth between T1-weighted images and pathological measurements was 1.11 mm, and the mean difference between T2-weighted images and pathological measurements was 2.17 mm; DOI: depth of invasion

Figure 3　BlandAltman map of the infiltration depth of tongue squamous cell carcinoma by T1- and T2-weighted imaging and pathologic measurements

图3　T1、T2加权成像与病理测量的舌鳞状细胞癌浸润深度的BlandAltman图



The pearson correlation coefficient r between T1-weighted images and pathology was 0.95 ($P < 0.001$). The correlation coefficient r between T2-weighted imaging and pathology was 0.92 ($P < 0.001$); DOI: depth of invasion

Figure 4　Correlation between T1- and T2-weighted MRI and the depth of invasion measured by pathology

图4　MRI中T1、T2加权成像与病理测量的浸润深度相关性

3　讨　论

口腔鳞状细胞癌是全球第12位常见癌症，也是排名第8位的癌症死亡病因，其中舌鳞状细胞癌发病率在全球范围内不断上升并趋于年轻化[9-10]。已有研究表明，与肿瘤部位、体积和宽度等因素相比，肿瘤的浸润深度是影响舌鳞状细胞癌颈淋巴结转移的最重要因素[11]。AJCC提出的第八版口腔癌TNM分期指南中浸润深度的定义与Jung[8]提出的浸润深度概念略有不同，其表面参考线由肿瘤两侧最邻近的正常黏膜交点连线修改为肿瘤与两侧最邻近的正常黏膜基底膜的交点的连线，并分别以5 mm和10 mm为界来区分肿瘤的T1与T2、T2与T3分类[12]。AJCC第八版口腔癌TNM分期使肿瘤的T分类由肿瘤最大直径和浸润深度共同决定，并且当临床或病理评价中如存在疑问时，应采取较低（或深度较浅）的T分期。第八版口腔癌TNM分期的改变使本研究中原第七版TNM分期里的T1分类患者和T2分类患者中各5名患者分别变为新版TNM分期中的T2、T3分类病人。

Lodder等[13]认为对早期的舌鳞状细胞癌（cT1-cT2），口内超声可获得较清晰的肿瘤成像，但超声测量的是肿瘤厚度，无法有效并直观获取肿瘤的

浸润深度。MRI是理想的软组织成像方法，采用脂肪抑制进一步提高软组织中肿瘤与炎症的鉴别能力[14]。本研究中T1加权成像对正常组织显像呈较高或等信号影，边界范围显像较T2加权成像清晰。T2加权成像较周围组织呈高信号影，对晚期舌鳞状细胞癌或血管生成丰富的舌鳞状细胞癌成像信号强，肿瘤边界常呈不规则信号影[15-16]。本研究MRI中T1加权成像测量的舌鳞状细胞癌浸润深度较病理结果平均高估1.11 mm，与病理结果的相关系数为0.95；T2加权成像平均高估2.17 mm，与病理结果的相关系数为0.92。大量的影像学观测发现核磁T2加权像较T1加权像不易区分肿瘤浸润边缘，更易高估肿瘤的浸润深度。Mao等[17]评估了核磁T2加权成像对舌鳞状细胞癌浸润深度测量的准确性，较病理平均高估2.32 mm；而Goel等[18]采用了T1加权成像中，测量的舌鳞状细胞癌浸润深度较病理平均高估1.62 mm。本研究同时检测了T1、T2加权序列并发现T1加权像较T2加权像与病理测量结果有更好的一致性和相关性。Jung等[8]和Yesuratnam等[19]研究认为，T2加权成像较T1加权像更易混淆舌鳞状细胞癌与其表面的水肿和炎症而造成高估。这些研究结果均表明T1加权成像更适合作为术前判断舌鳞状细胞癌的浸润深度的方法，与本研究发现一致。

本研究中MRI设备均采用1 mm层厚的薄层扫描，以防止过大的扫描厚度错失影像中肿瘤的最大浸润深度而使测量的准确性变差。此外，大部分先前的研究中核磁场强为1T或1.5T，本研究中MR设备采用3T场强。Preda等[20]认为采用高的核磁场强度可提高MRI成像分辨率，提高测量的准确性。此外，同样有研究表明高的磁场强度会产生高的信噪比、磁化对比度和光谱分辨率，从而获得更好的MR成像质量[21-23]。本研究为了避免肿瘤在成像至手术间隔内的浸润生长所带来的的误差，所有病人的影像检查和手术时间间隔均小于10 d（肿瘤指南为31 d）。值得注意的是，患者的术前活检可能会影响病理测量的结果。MRI检查时间较长，尤其是T2加权成像，检查期间因患者舌移位和吞咽易导致成像模糊和伪影。因此，临床医生应在MRI影像检查前告知患者保持头后仰不偏斜，避免吞咽和说话，以防止舌偏斜对测量差生误差。此外，舌鳞状细胞癌标本切除后会失血萎缩，可能是病理测量的浸润深度均值低于MRI的主要原因[24]，如何量化萎缩量有待进一步研究。

综上所述，MRI测量的舌鳞状细胞癌浸润深度较为准确，与病理测量结果相比有平均高估1～2 mm，其中T1加权像是较为准确的影像参考。

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参考文献

[1] Cariati P, Cabello SA, Fernandez SJ, et al. Distribution of cervical metastasis in tongue cancer: are occult metastases predictable? A retrospective study of 117 oral tongue carcinomas[J]. J Craniomaxillofac Surg, 2018, 46(1): 155 - 161. doi: 10.1016/j.jcms.2017.10.009.

[2] Ahmed SQ, Junaid M, Awan S, et al. Frequency of cervical nodal metastasis in early-stage squamous cell carcinoma of the tongue[J]. Int Arch Otorhinolaryngol, 2018, 22(2): 136-140. doi: 10.1055/s-0037-1603626.

[3] Kaul P, Poonia DR. Tumor budding and adjacent tissue at the invasive front correlate with delayed neck metastasis in clinical early-stage tongue squamous cell carcinoma[J]. J Surg Oncol, 2019, 119(3): 370-378. doi: 10.1002/jso.25772.

[4] Faisal M, Abu Bakar M, Sarwar A, et al. Depth of invasion (DOI) as a predictor of cervical nodal metastasis and local recurrence in early stage squamous cell carcinoma of oral tongue (ESSCOT)[J]. PLoS One, 2018, 13(8): e0202632. doi: 10.1371/journal.pone.0202632.

[5] Almangush A, Bello IO, Coletta RD, et al. For early-stage oral tongue cancer, depth of invasion and worst pattern of invasion are the strongest pathological predictors for locoregional recurrence and mortality[J]. Virchows Arch, 2015, 467(1): 39 - 46. doi:10.1007/s00428-015-1758-z.

[6] Berdugo J, Thompson L, Purgina B, et al. Measuring depth of invasion in early squamous cell carcinoma of the oral tongue: positive deep margin, extratumoral perineural invasion, and other challenges[J]. Head Neck Pathol, 2019, 13(2): 154 - 161. doi: 10.1007/s12105-018-0925-3.

[7] Pentenero M, Gandolfo S, Carrozzo M. Importance of tumor thickness and depth of invasion in nodal involvement and prognosis of oral squamous cell carcinoma: a review of the literature[J]. Head Neck, 2005, 27(12): 1080-1091. doi: 10.1002/hed.20275.

[8] Jung J, Cho NH, Kim J, et al. Significant invasion depth of early oral tongue cancer originated from the lateral border to predict regional metastases and prognosis[J]. Int J Oral Maxillofac Surg, 2009, 38(6): 653-660. doi: 10.1016/j.ijom.2009.01.004.

[9] Johnson NW, Jayasekara P, Amarasinghe AA. Squamous cell carcinoma and precursor lesions of the oral cavity: epidemiology and aetiology[J]. Periodontol 2000, 2011, 57(1): 19-37. doi: 10.1111/j.1600-0757.2011.00401.x.

[10] Patel SC, Carpenter WR, Tyree S, et al. Increasing incidence of oral tongue squamous cell carcinoma in young white women, age 18 to 44 years[J]. J Clin Oncol, 2011, 29(11): 1488 - 1494. doi:

10.1200/JCO.2010.31.7883.

[11] Yuen AP, Lam KY, Wei WI, et al. A comparison of the prognostic significance of tumor diameter, length, width, thickness, area, volume, and clinicopathological features of oral tongue carcinoma[J]. Am J Surg, 2000, 180(2): 139-143. doi: 10.1016/s0002-9610(00)00433-5.

[12] 尚伟, 郑家伟. 口腔及口咽癌新版TNM分期与NCCN诊治指南部分解读[J]. 中国口腔颌面外科杂志, 2018, 16(6): 533-546. doi: 10.19438/j.cjoms.2018.06.010.
Shang W, Zheng JW. Partial interpretation of the new TNM staging and NCCN diagnosis and treatment guidelines for oral and oropharyngeal cancer[J]. J Oral Maxillofac Surg, 2018, 16(6): 533-546. doi: 10.19438/j.cjoms.2018.06.010.

[13] Lodder WL, Hauptmann M, Teertstra HJ, et al. Is preoperative ultrasonography accurate in measuring tumor thickness and predicting the incidence of cervical metastasis in oral cancer?[J]. Oral Oncol, 2009, 46(1): 38-41. doi: 10.1016/j.oraloncology.2009. 10.005.

[14] Kalovidouri A, Firmenich N, Delattre B, et al. Fat suppression techniques for breast MRI: dixon versus spectral fat saturation for 3D T1-weighted at 3T[J]. Radiol Med, 2017, 122(10): 731-742. doi: 10.1007/s11547-017-0782-2.

[15] Park JO, Jung SL, Joo YH, et al. Diagnostic accuracy of magnetic resonance imaging (MRI) in the assessment of tumor invasion depth in oral/oropharyngeal cancer[J]. Oral Oncol, 2011, 47(5): 381-386. doi: 10.1016/j.oraloncology.2011.03.012.

[16] Ross MR, Schomer DF, Chappell P, et al. MR imaging of head and neck tumors: comparison of T1-weighted contrast-enhanced fat-suppressed images with conventional T2-weighted and fast spin-echo T2-weighted images[J]. AJR Am J Roentgenol, 1994, 163(1): 173-178. doi: 10.2214/ajr.163.1.8010208.

[17] Mao MH, Wang S, Feng Z, et al. Accuracy of magnetic resonance imaging in evaluating the depth of invasion of tongue cancer. A prospective cohort study[J]. Oral Oncol, 2019, 91(91): 79-84. doi: 10.1016/j.oraloncology.2019.01.021.

[18] Goel V, Parihar PS, Parihar A, et al. Accuracy of MRI in prediction of tumour thickness and nodal stage in oral tongue and gingivobuccal cancer with clinical correlation and staging[J]. J Clin Diagn Res, 2016, 10(6): TC01-TC05. doi: 10.7860/JCDR/2016/17411.7905.

[19] Yesuratnam A, Wiesenfeld D, Tsui A, et al. Preoperative evaluation of oral tongue squamous cell carcinoma with intraoral ultrasound and magnetic resonance imaging-comparison with histopathological tumour thickness and accuracy in guiding patient management[J]. Int J Oral Maxillofac Surg, 2014, 43(7): 787-794. doi: 10.1016/j.ijom.2013.12.009.

[20] Preda L, Chiesa F, Calabrese L, et al. Relationship between histologic thickness of tongue carcinoma and thickness estimated from preoperative MRI[J]. Eur Radiol, 2006, 16(10): 2242-2248. doi: 10.1007/s00330-006-0263-9.

[21] Moreno KF, Cornelius RS, Lucas FV, et al. Using 3 tesla magnetic resonance imaging in the pre-operative evaluation of tongue carcinoma[J]. J Laryngol Otol, 2017, 131(9): 793-800. doi: 10.1017/S0022215117001360.

[22] Lam P, Au-Yeung KM, Cheng PW, et al. Correlating MRI and histologic tumor thickness in the assessment of oral tongue cancer[J]. AJR Am J Roentgenol, 2004, 182(3): 803-808. doi: 10.2214/ajr.182.3.1820803.

[23] Schmitt F, Grosu D, Mohr C, et al. 3 Tesla MRI: successful results with higher field strengths[J]. Radiologe, 2004, 44(1): 31-47. doi: 10.1007/s00117-003-1000-x.

[24] Smiley N, Anzai Y, Foster S, et al. Is ultrasound a useful adjunct in the management of oral squamous cell carcinoma?[J]. J oral maxillofac Surg, 2019, 77(1): 204-217. doi: 10. 1016/j.joms.2018.08.012.

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