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Research article

Differentiating between benign and malignant sinonasal lesions using dynamic contrast-enhanced MRI and intravoxel incoherent motion

Jingxuan Jiang[a,b], Zebin Xiao[c,1], Zuohua Tang[c,*], Yufeng Zhong[a], Jinwei Qiang[a,**]

[a] Department of Radiology, Jinshan Hospital, Fudan University, Shanghai 201508 China
[b] Department of Radiology, Affiliated Hospital of Nantong University, Nantong 226001, China
[c] Department of Radiology, Eye and ENT Hospital, Fudan University Shanghai, 200031, China

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ABSTRACT

Purpose: To explore the value of dynamic contrast-enhanced MRI (DCE-MRI) and intravoxel incoherent motion (IVIM) for distinguishing between benign and malignant sinonasal lesions and investigate the correlations between the two methods.

Methods and materials: Patients with sinonasal lesions (42 benign and 31 malignant) who underwent DCE-MRI and IVIM before confirmation by histopathology were enrolled in this prospective study. Parameters derived from DCE-MRI and IVIM were measured, the optimal cut-off values for differential diagnosis were determined, and the correlations between the two methods were evaluated. Statistical analyses were performed using the Wilcoxon rank sum test, receiver operating characteristic (ROC) curve analysis, and Spearman's rank correlation.

Results: Significantly higher K^{trans} and K_{ep} values but lower D and f values were found in malignant lesions than in benign lesions (all $p < 0.001$). There were no significant differences in the V_e and D* values between the two groups. The area under the curve (AUC) of K^{trans} was significantly higher than those of other parameters. There was no significant difference between the AUCs of DCE-MRI and IVIM with parameters combined ($p = 0.86$). Significant inverse but weak correlations were found between D and K^{trans} ($r = -0.46$, $p < 0.001$), f and K^{trans} ($r = -0.41$, $p < 0.001$), D and K_{ep} ($r = -0.37$, $p = 0.008$), and f and K_{ep} ($r = -0.33$, $p = 0.004$).

Conclusions: DCE-MRI and IVIM can effectively differentiate between benign and malignant sinonasal lesions. IVIM findings correlate with DCE-MRI results and may represent an alternative to DCE-MRI.

1. Introduction

Neovascularization is necessary for tumor growth, invasion, and metastasis [1]. Local microvascular perfusion is an important feature for the diagnosis and differentiation of sinonasal lesions [2]. Although conventional contrast-enhanced magnetic resonance imaging (MRI) provides a non-quantitative method for evaluating the blood supply of tissues and organs, the evaluation criteria are subjective [3], and the potential overlap of enhancement appearances between benign and malignant lesions decreases the precision of the technique for differentiating malignant from benign sinonasal lesions [4]. For example, fibromas and inflammatory lesions show intense enhancement, which can lead to their misdiagnosis as malignant tumors [5,6].

Novel imaging techniques, such as the quantitative dynamic contrast-enhanced MRI (DCE-MRI), have been widely used for distinguishing malignancies from benign lesions and monitoring treatment response in the head and neck [7,8]. In previous studies of head and neck lymph nodes, brain tumors, and breast lesions, quantitative DCE-MRI was shown to be useful for distinguishing between benign and malignant lesions [9,10]. A pharmacokinetic model was proposed by Tofts et al. [11] to quantitatively determine the capillary blood flows in tumors. This model includes calculation of the volume transfer constant (K^{trans}), reverse rate constant (K_{ep}), and extravascular extracellular volume fraction (V_e). K^{trans} quantifies the diffusion of the contrast agent from the blood plasma through the capillary wall into the extravascular extracellular space (EES); K_{ep} quantifies the diffusion of the contrast agent from the EES back to the plasma; V_e reflects the volume of the EES [12]. DCE-MRI can describe the complicated microcirculation in living tissues and provide quantitative information about vascular permeability and angiogenesis. However, it cannot provide perfusion information without the use of contrast agents, which is particularly relevant in patients who cannot tolerate gadolinium contrast agents

* Corresponding author at: Department of Radiology, Eye and ENT Hospital, Fudan University. Address: 83 Fenyang Road, Shanghai, 20031, China.
** Corresponding author at: Department of Radiology, Jinshan Hospital, Fudan University. Address: 1508 Longhang Road, Shanghai, 201508, China.
E-mail addresses: tzh518sunny@163.com (Z. Tang), dr.jinweiqiang@163.com (J. Qiang).
[1] Jingxuan Jiang and Zebin Xiao are co-first authors, who contribute equally to this study.

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[13].

Le Bihan et al. [14] first proposed intravoxel incoherent motion (IVIM), which can be sensitive to both water diffusion behavior and capillary perfusion. This model includes calculations of diffusivity (D), pseudo-diffusivity (D*), and vascular volume fraction (f). D quantifies pure water diffusion in the tissue, D* reflects the perfusion-related incoherent microcirculation; and f is the microvascular volume fraction within the lesion [15]. IVIM has shown great potential in reflecting diffusivity and microvascular perfusion of tissues without the use of contrast agents [16,17].

To the best of our knowledge, no studies on DCE-MRI and IVIM in the sinus and nasal cavity have been performed to date. In this study, we aimed to explore DCE-MRI and IVIM as tools for distinguishing between benign and malignant sinonasal masses and to investigate the correlation between the two methods.

2. Materials and methods

2.1. Patients

The institutional review board of the Eye and ENT Hospital of Fudan University approved this study. Between May 2015 and December 2015, 73 patients (25 females and 48 males; mean age of 53.4 years) with sinonasal solid masses were recruited. The masses were confirmed by biopsy or surgery, and pathology. Patients with a history of biopsy, surgery and chemotherapy were excluded. Of the 73 patients, 42 patients had malignant lesions, and 31 had benign lesions. The malignant lesions included squamous cell carcinoma (n = 16), olfactory neuroblastoma (n = 7), adenoid cystic carcinoma (n = 4), rhabdomyosarcoma (n = 5), melanoma (n = 5), lymphoma (n = 2), undifferentiated carcinoma (n = 1), malignant fibrohistiocytoma (n = 1), and osteosarcoma (n = 1). Benign lesions included inflammatory polyps (n = 18), papilloma (n = 7), spindle cell tumor (n = 3), fibrous tumor of the bone (n = 2), and enamel cell tumor (n = 1).

2.2. MRI scan protocol

All MRI scans were performed on a 3T MRI scanner (Verio; Siemens Healthcare, Erlangen, Germany). Before performing DCE-MRI, routine T1WI, T2WI and IVIM data were acquired. As demonstrated in Table 1, IVIM was performed using single-shot echo-planar imaging with parameters as follows: time of repetition (TR)/time of echo (TE) = 5200 ms/83 ms, field of view (FOV) = 230 mm, slices = 5, slice thickness = 5 mm, 13 b-factors: 0, 50, 100, 150, 200, 250, 300, 350, 400, 800, 1000, 1500, 2000, and 2500 s/mm^2, number of averages = 2. The total scan time for IVIM was 6 min 42 s. DCE-MRI parameters were as follows: TR/TE = 7.52 ms/2.06 ms, flip angle = 15°, number of excitation = 1, FOV = 220 mm, slice thickness = 5 mm, temporal resolution = 7 s/dynamic, number of dynamics = 30. The total DCE-MRI scanning time was 3 min 43 s. After the acquisition of two baseline scans, DCE-MRI was performed after intravenous administration of 0.1 mmol/kg gadopentetate dimeglumine (Gd-DTPA, Magnevist, Bayer Schering, Berlin, Germany) at a rate of 3 mL/s, followed by 20 mL of 0.9% saline flush.

2.3. Image analysis

DCE-MRI processing was performed using a commercial software (Tissue 4D; Siemens Healthcare, Erlangen, Germany). An appropriate artery was semiautomatically selected to characterize the input function curve and concentration-time curve for setting the arterial input function (AIF) [11]. We used the perfusion analysis method based on the most common used 2-compartment pharmacokinetic model which was proposed by Tofts et al. [11] to calculate pharmacokinetic parameters, including K^{trans}, K_{ep} and V_e.

IVIM processing was conducted by using Mathlab program (MathWorks, Inc, Natick, MA), and the IVIM images were performed auto-correction. IVIM model is mathematically expressed as follows: $S_b/S_0 = (1\text{-}f)\ e^{-bD} + fe^{-b(D+D^*)}$ [14], where S_b and S_0 are the signal intensity in the diffusion gradient factors of b and 0, respectively. f is the fractional volume of capillary blood, D is the diffusion coefficient and D* is the perfusion-related diffusion coefficient. For each pixel, the upper and lower limits were set for f and D* values to exclude unrealistic measurements (probably because of several outliers) and avoid including any erroneous pixels in the calculation. The lower and upper limits of f and D* were respectively set at 0%-40% and 0–50 × 10^{-3} mm^2/s by referring to an earlier report [18].

DCE-MRI (K^{trans}, K_{ep} and V_e) and IVIM (D, D* and f) parameters were measured independently by two radiologists (JXJ. and YFZ., who have 4 and 3 years of experience in head and neck imaging, respectively) who were blinded to clinical and histopathological data. The oval regions of interest (ROIs), ranging from 20 to 50 mm^2 in size, were drawn in homogeneous enhancement regions by avoiding necrotic tissues, vessels, and dominant ducts as large as possible, and the normal

Table 1
Sequence Parameters of IVIM and DCE-MRI.

	IVIM
Acquisition plane	Axial
Acquisition scheme	Free breathing SS EPI
TR	5200
TE	83
b-values (sec/mm^2)	0,50,100,150,200,250,300,350,400,800,1000,1500,2000,2500
Field of view (mm)	230
Slice thickness	5
Interslice gap (mm)	5
Number of slices Parallel imaging factor	6
Number of averages	2
Scan time (min)	6 min 42 s
	DCE-MRI
Acquisition plane	Axial
TR	7.52
TE	2.06
Flip angle	15
FOV Read (mm)	220
Slice thickness (mm)	5
Number of slices Parallel imaging factor	6
Number of averages	1
Scan time (min)	3 min 43 s

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