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Application of Intravoxel Incoherent Motion (IVIM) Model for Differentiation Between Metastatic and Non-Metastatic Head and Neck Lymph Nodes

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
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G Funds Collection

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Summary

Background: Application of intravoxel incoherent motion (IVIM) model parameters, including: true diffusion (D), pseudodiffusion (D*), and perfusion fraction (Fp), for differentiation between metastatic and non-metastatic head and neck lymph nodes.

Material/Methods: Diffusion-weighted images/apparent diffusion coefficient (DWI/ADC) images of 86 lymph nodes from 31 cancer patients were analyzed. DWI images were obtained with a 1.5T MRI scanner (Magnetom Avanto); b=0,50, 150, 300, 500, 750, 1000, 1200 s/mm^2.

Results: In the study group, there were 32 (37%) and 54 (67%) metastatic and non-metastatic lymph nodes, respectively. The mean values of D, D*, and Fp did not differ significantly between metastatic and non-metastatic lymph nodes.

Conclusions: IVIM parameters are not useful for differentiation between metastatic and non-metastatic head and neck lymph nodes.

MeSH Keywords: Head and Neck Neoplasms • Lymph Nodes • Lymphatic Metastasis

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Background

A precise determination of nodal involvement is important for staging and critical for optimal planning of treatment in patients with head and neck carcinoma (HNC). The differentiation between normal (non-metastatic) and metastatic lymph nodes (especially when not enlarged), based only on palpation, is usually difficult, and it is often not possible at all in some nodal localizations. Considering the shape and dimensions of lymph nodes, standard MRI or CT scans do not always distinguish between metastatic and normal lymph nodes. Currently, new noninvasive methods are needed for an accurate characterization of both primary tumors of the head and neck and nodal metastases. This characterization is critical for planning individualized treatment and for improved management of cancer patients. Diffusion-weighted imaging (DWI) is a new technique that may help to detect metastatic lymph nodes and differentiate them from non-metastatic lymph nodes.

Intravoxel incoherent motion (IVIM), initially described by Le Bihan et al. [1], is an advanced imaging technique that separates diffusion and perfusion by calculating several diffusion- and perfusion-related parameters. In DWI, tissue signal attenuation that is observed with increasing b values, reflects tissue diffusivity, which reduces the effect of

Table 1. Parameters of MR algorithms together with DWI-MR.

Type of sequence	Attenuation of the signal by adipose tissue	Plane	TR (time repetition) TE (time echo)	Thickness of the layer/distance between layers	Matrix
Images T2 dependent TSE (Turbin Spin Echo)	Yes	Transversal	TR=4480 ms TE=68 ms	3.0/1.0 mm	256×256
Images T2 dependent TSE (Turbin Spin Echo)	No	Transversal	TR=313 ms TE=92 ms	3.0/1.0 mm	256×256
Images DWI EPI (Spin Echo) **b 0, 50, 150, 300, 500, 750, 1000, 1200**	Yes	Transversal	TR=3200 ms TE=88 ms	4.0/1.2 mm	192×192
Dynamic Examination Images T1 dependent GRE (Gradient Echo)	Yes	Transversal	TR=5.5 ms TE=2.4mm	1.1/03 mm	256×256
Images T1 dependent CM	Yes	Transversal	TR=585 ms TE=9.2 ms	3.0/1.0 mm	512×512

tissue microcapillary perfusion. This signal attenuation can be measured quantitatively. The most common quantitative evaluation of DWI is provided by the apparent diffusion coefficient (ADC). ADC values are influenced by both tissue diffusivity and pseudorandom motion caused by microcapillary perfusion, also known as pseudodiffusion.

It has been generally accepted that microperfusion affects signal values measured with low values of the b coefficient [1–3]. Optimal b threshold values, between the true diffusion (D), pseudodiffusion (D*), and perfusion fraction (Fp), have not been unequivocally determined to date; b=200 s/mm^2 has been reported most commonly [2,4–8]. In this study, we attempted to differentiate between metastatic and normal lymph nodes, based on the values of D*, Fp, and D.

Material and Methods

MRI scans of 86 neck lymph nodes, obtained from 31 cancer patients, were analyzed. In all lymph nodes, a diagnosis was confirmed by a histopathological or cytological examination. Almost all patients (29/31, 93.5%) had HNC, and MRI was performed for staging before treatment. In 2 (6.5%) patients from this group, metastases from an unknown primary source were diagnosed. In this study group, there were 49% of men and 51% of women; the mean age was 58 years (range: 25–71 years); most patients were had 61–70 years. Among a total of 86 lymph nodes, there were 32 (37%) metastatic and 54 (67%) non-metastatic nodes, respectively. All MRI scans were performed in the Radiodiagnostic Department of the Center of Oncology, Institute Maria Skłodowska-Curie Memorial, Gliwice branch, Poland.

A 1.5T MRI scanner (Magnetom Avanto, Siemens, Erlangen, Germany), with a head and neck coil was used to obtain all MR images. The standard MRI protocol for head and neck lesions (used in our institution for HNC) was applied.

Algorithms that were used are presented in Table 1.

Macroscopic descriptions of surgical specimens were used for confirmation of the topography of resected lymph nodes that had been revealed on MRI. Subsequently, dimensions and distances from characteristic anatomical structures (parotid glands, mandibular glands, and MSO) were assessed.

D*, D, and Fp were calculated according to the equation proposed by Le Bihan in the IVIM model [2,6,9,10].

As previously mentioned, tissue signal attenuation in DWI that is observed with increasing b values, reflects tissue diffusivity and reduces the effect of tissue microcapillary perfusion. This signal attenuation can be measured quantitatively. The most common quantitative evaluation of DWI is ADC, which has been used for characterization of both normal and pathological tissues. ADC has been used in diagnosis, prognosis, and treatment monitoring in patients with tumors arising from various sites. However, ADC values are influenced by both tissue diffusivity and pseudorandom motion, which is caused by microcapillary perfusion. The perfusion effect is difficult to eliminate. The IVIM technique estimates parametric values of those effects separately, measuring DWI across multiple b values and employing biexponential fitting.

The biexponential model best fits the description of signal intensity and b coefficient value correlation.

$$S_i = S_{fit}[(1-F_p)e^{-b_i D} + F_p e^{-b_i D^*}]$$

S_i – the measured signal intensity with diffusion weighting b
S_{fit} – signal intensity for b=0
F_p – pseudodiffusion fraction
D – the true diffusion coefficient
D* – pseudodiffusion coefficient

In this model, the first exponent describes signal attenuation caused by true diffusion, and the second one describes signal attenuation caused by pseudodiffusion.

Table 2. True diffusion coefficient (D) values for b 300 – b 1200 in both groups of lymph nodes.

Lymph nodes	D values				Sd
	Mean $\times 10^{-3}\left[\frac{mm^2}{s}\right]$	Median $\times 10^{-3}\left[\frac{mm^2}{s}\right]$	Min. value $\times 10^{-3}$	Max. value $\times 10^{-3}\left[\frac{mm^2}{s}\right]$	
Metastatic	0.652	0.640	0.310	1.21	± 0.19
Nonmetastatic	0.686	0.650	0.320	1.13	± 0.20

Table 3. Perfusion fraction (F_p) values in both groups of lymph nodes.

Lymph nodes	F_p (%) values				Sd
	Mean	Median	Minimum	Maximum	
Metastatic	18.1	14.7	3.4	53.6	± 10.7
Nonmetastatic	21.8	19.3	5.9	61	± 13.6

The perfusion fraction is a quantitative estimate of the contribution of microperfusion to the signal loss in DWI.

To determine the parameters, i.e., S_{fit}, F_p, D, and D*, MatLab programming tools were used, including an option of function fitting with the defined characteristics to the values determined empirically. However, since the fitting of all parameters in this equation (with four unknown variables) can be problematic, especially in the case of low perfusion or with small number of measurements, for various b values (most often used for calculation of the perfusion fraction) an algorithm was used that was based on monoexponential fitting of the signal attenuation curve. Similar algorithm was used for higher b values (typically b >100 s/mm^2), assuming that, above the determined b value, signal attenuation is affected by the extracapillary factor (true diffusion) only.

$$S_i = S_{exp} e^{-b_i D}$$

S_{exp} has been extrapolated for b=0 s/mm^2 value of the signal, determined by fitting of the exponential curve for b >100 s/mm^2.

S_{exp} estimation enables to assess perfusion fraction (Fp) according to the model

$$3F_p = S_0 - S_{exp}/S_0$$

S_0 – signal value for b=0 s/mm^2

Results

The true diffusion coefficient was calculated as a fit of a monoexponential curve to the measured signal values of b >300 s/mm^2.

$$S_x = S_{ext} e^{-bxD}$$

S_x – signal intensity for b >300 s/mm^2
b_x – coefficient b value
D – true diffusion coefficient

In this particular model, a simultaneous calculation of two unknown values, S_{ext} and D, was possible (as presented in Table 2).

The mean, median, maximal, and minimal D values in both groups of lymph nodes were comparable.

These true diffusion coefficient values were similar in both groups, as confirmed by the Mann-Whitney U test (p=0.5220).

The perfusion fraction, which indicates the percentage of perfusion in the decrease of signal intensity, was calculated from DWI images, with an increase of b values according to the following equation:

$$F_p = \frac{S_o - S_{ext}}{S_o}$$

in which:

S_o – signal intensity for b=0 s/mm^2 (Table 3).

Based on the Mann-Whitney U test, the mean values of perfusion fraction (F_p) were similar in both groups of lymph nodes (p=0.2940).

The pseudodiffusion coefficient was calculated as a biexponential curve fit, using the following model:

$$S_x = S_o[(1 - F_p)e^{-bxD} . F_p e^{-bxD}]$$

in which:

S_x – signal intensity for b >0 s/mm^2
S_o – signal intensity for b=s/mm^2
D – true diffusion
*D** – pseudodiffusion
b_x – b coefficient value
F_p – perfusion fraction

D* values for both groups of lymph nodes are presented in Table 4.

Table 4. Pseudodiffusion values (D*) in both groups of lymph nodes.

Lymph nodes	D* values				Sd
	Mean $\times10^{-3}$ mm^2/s	Median $\times10^{-3}$ mm^2/s	Minimum $\times10^{-3}$ mm^2/s	Maximum $\times10^{-3}$ mm^2/s	
Metastatic	11.9	7.8	3.2	45.1	± 10.2
Nonmetastatic	15.5	9.8	3.6	44.3	± 12.7

As in the case of previously calculated parameters (D and Fp), the mean values of pseudodiffusion coefficients, in both groups of lymph nodes, were similar (based on the Mann-Whitney U test; p=0.3046)

Discussion

Neoangiogenesis and increased perfusion are characteristic features of malignant tumors. It is interesting, whether these features could be used for differentiation between metastatic and non-metastatic lymph nodes.

True diffusion of water particles in the extravascular/extracellular compartment, together with blood movement in the capillary vessels (that mimics diffusion), influence diffusion spectra [1,11,12].

The IVIM model has been implemented for differentiation between malignant and benign lesions, based on their cellular density (D), taking into consideration perfusion (Fp, D*) as a marker of tumor vascularization [7].

DWI spectra obtained with low b values are primarily affected by perfusion, although a specific b (s/mm^2) threshold value has not been commonly accepted yet.

The b coefficient value of 200 s/mm^2 has been accepted by most authors as a threshold value for pseudodiffusion [1,5,6,11,13]. Most studies, that reported the clinical use of IVIM parameters, investigated tumors of the brain, liver, breast, and prostate. However, studies exploring the IVIM model for head and neck cancer are sparse.

Recently, Sumi et al. reported the results of an analysis of 123 head and neck tumors in 118 patients. Using the IVIM model, 6 various tumor types, including squamous carcinoma, lymphoma, neuroma, Warthin tumor, adenocarcinoma, and benign neck tumors, were described. The highest, moderate and lowest pseudodiffusion parameters were observed in malignant salivary gland tumors, squamous cell carcinoma, and lymphoma, respectively [14].

According to those authors, various IVIM spectra were dependent on different histological tumor structures, and most importantly, on the quantity of extracellular tissue stroma. For instance, malignant tumors originating from the salivary glands consisted of nests of cancer cells with abundant blood vessels. Various quantities of stroma tissue with neoangiogenesis was a typical feature of the squamous cell cancer. In contrast, lymphomas consisted mostly of intensively dividing, tightly packed, neoplastic cells without much stroma between them.

The IVIM model, as a tool for assessing treatment results in patients with HNC, has been recently reported by Hauser. For primary and metastatic tumors with a high perfusion fraction or a high ADC value on initial examination, treatment responses were significantly worse. High initial ADC values usually reflected necrosis that might explain poor responses to radiotherapy or chemotherapy [10,15].

Lymph nodes with increased vascularization (i.e. increased perfusion fraction) were observed in patients with HNC who failed treatment [10].

The true diffusion coefficient was similar in the case of persistent neck nodes (D=0.88–0.97$\times10^{-3}$ mm^2/s) and in the cured patients (D=0.64–0.88$\times10^{-3}$mm^2/s) (p=0.30). Based on the IVIM model, primary pharyngeal tumors and metastatic lymph nodes were compared by Lu et al. In that study, significantly lower values of perfusion fraction and higher true diffusion coefficient values were observed in metastatic nodes, in comparison to the primary pharyngeal tumors [16].

Also, using the IVIM model, some malignant tumors (squamous cell carcinoma, adeno-cystic carcinoma, and pleomorphic adenocarcinoma) and benign tumors (mixt tumor, myoepithelial tumor, and vascular malformation) were compared by Sakamoto et al. According to their report, significantly lower values of ADC and true diffusion coefficients as well as higher values of pseudodiffusion coefficients were observed in malignant tumors. However, the perfusion fraction was similar in both groups of tumors [18].

In summary, in this study, the values of D, D*, and Fp in all lymph nodes were calculated and compared. These parameters did not differ significantly between metastatic and non-metastatic groups of lymph nodes. In addition, the mean values of true diffusion coefficient (p=05220), perfusion fraction (p=0.2940), and pseudodiffusion (p=0.3046) were comparable in both groups. It should be noted that the values of true diffusion coefficient and perfusion fraction, calculated in our study for the metastatic nodes, were comparable to those reported by Hauser and Lu [10,16].

Conclusions

Pseudodiffusion, perfusion fraction and true diffusion should not be used for differentiation between metastatic and non-metastatic lymph nodes.

References:

1. Le Bihan D, Breton E, Lallemand D et al: Separation of diffusion and perfusion intravoxel incohorent motion MR imaging. Radiology, 1988; 168: 497–505
2. Koh DM, Thoeny HC: Diffusion – weighted MR imaging. Applicatins in the body. Springer, 2010; 33–47, 137–38, 169, 187–200
3. Barbero JPM, Jiménez IR, Noguerol TM et al: Utility of MRI diffusion techniques in the tumors of the head and neck. Cancers, 2013; 5: 875–89
4. Padhani A, Liu G, Mu-Koh D et al: Diffusion-weighted magnetic resonance imaging as a cancer biomarker: consensus and recommendations. Neoplasia, 2009; 11: 102–25
5. Riches SF, Hawtin K, Charles-Edwards EM et al: Diffusion-weighted imaging of the prostate and rectal wall: Comparison of biexponential and monoexponential modeled diffusion and associated perfusion coefficients. NMR Biomed, 2009; 22: 318–25
6. Bisdas S, Koh T, Roder C et al: Intravoxel incoherent motion diffusion-weighted MR imaging of gliomas: Feasibility of the method and initial results. Neuroradiology, 2013; 55: 1189–96
7. Kang K, Lee J, Yoon J et al: Intravoxel incohorent motion diffusion-weighted MR imaging for characterization of focal pancreatic lesions. Radiology, 2014; 270: 444–53
8. Sakamoto J, Imaizumi A, Sasaki Y et al: Comparison of accuracy of intravoxel incoherent motion and apparent diffusion coefficient techniques for predicting malignancy of head and neck tumor using half-Fourier single-shot turbo spin-echo diffusion-weighted imaging. Magn Reson Imaging, 2014; 32: 860–66
9. Thoeny HC, De Keyzer F, King AD: Diffusion-weighted MR imaging in the head and neck. Radiology, 2012; 263: 19–31
10. Hauser T, Essig M, Jensen A et al: Prediction of treatment response in head and neck carcinomas using IVIM-DWI: Evaluation of lymph node metastasis. Eur J Radiol, 2014; 83: 783–87
11. Hermans R: Diffusion-weighted MRI in head and neck cancer. Curr Opin Otolaryngol Head Neck Surg, 2010; 18(2): 72–78
12. Andreou A, Koh D, Collins D et al: Measurement reproducibility of perfusion fraction and pseudodiffusion coefficient derived by intravoxel incoherent motion diffusion-weighted MR imaging in normal liver and metastases. Eur Radiol, 2013; 23: 428–34
13. Shinmoto H, Oshio K, Tanimoto A et al: Biexponential apparent diffusion coefficients in prostate cancer. Magn Reson Imaging 2009; 27: 355–59
14. Sumi M, Nakamura T: Head and neck tumors: Assessment of perfusion-related parameters and diffusion coefficient based on the intravoxel incohorent motion model. Am J Neuroradiol, 2013; 34(2): 410–16
15. Hauser T, Essig M, Jensen A et al: Characterization and therapy monitoring of head and neck carcinomas using diffusion-imaging-based intravoxel incoherent motion parameters – preliminary result. Neuroradiology, 2013; 55: 527–36
16. Lu Y, Jansen J, Stambuk H et al: Comparing primary tumors and metastatic nodes in head and neck cancer using intravoxel incoherent motion imaging: A preliminary experience. J Comput Assist Tomogr, 2013; 37: 1–17