RESEARCH ARTICLE

Quantitative dynamic contrast-enhanced and diffusion-weighted MRI for differentiation between nasopharyngeal carcinoma and lymphoma at the primary site

^{1,2}Xiao-ping Yu, ¹Jing Hou, ¹Fei-ping Li, ¹Wang Xiang, ¹Qiang Lu, ³Yin Hu and ³Hui Wang

¹Department of Diagnostic Radiology, Hunan Cancer Hospital and the Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, Hunan, People's Republic China; ²Department of Radiology, the third Xiangya Hospital, Central South University, Changsha, Hunan, People's Republic China; ³Department of Diagnostic Radiotherapy, Hunan Cancer Hospital and the Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, Hunan, People's Republic China

Objectives: To investigate the value of quantitative dynamic contrast-enhanced MRI (QDCE-MRI) and diffusion-weighted MRI (DW-MRI) in differentiating nasopharyngeal carcinoma (NPC) from lymphoma.

Methods: We retrospectively analysed the data from 102 patients (82 with NPC and 20 with lymphoma) who underwent pre-treatment QDCE-MRI and DW-MRI on a 1.5-T MR unit. QDEC-MRI parameters [influx transfer constant (K^{trans}), efflux rate constant (K_{ep}), fractional volume of extravascular extracellular space (V_e) and fractional volume of plasma (f_{PV})] based on pharmacokinetic model and apparent diffusion coefficient (ADC) were compared between the two nasopharyngeal malignancies.

Results: The K^{trans} , K_{ep} , V_e , f_{PV} and ADC values (mean $\pm$ standard deviation) for NPC were $0.366 \pm 0.155 \text{ min}^{-1}$, $1.353 \pm 0.468 \text{ min}^{-1}$, 0.292 ± 0.117 , 0.027 ± 0.024 and $0.981 \pm 0.184 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$, respectively. The K^{trans} , K_{ep} , V_e , f_{PV} and ADC values (mean $\pm$ standard deviation) for lymphoma were $0.212 \pm 0.059 \text{ min}^{-1}$, $1.073 \pm 0.238 \text{ min}^{-1}$, 0.213 ± 0.104 , 0.008 ± 0.007 and $0.760 \pm 0.182 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$, respectively. Optimal cut-off values (area under the curve, sensitivity, specificity) for distinguishing the two tumours were as follows: $K^{\text{trans}} = 0.262 \text{ min}^{-1}$ (0.866, 80.49%, 85.00%), $K_{\text{ep}} = 1.401 \text{ min}^{-1}$ (0.681, 43.90%, 100.00%), $V_e = 0.211$ (0.784, 76.83%, 85.00%), $f_{\text{PV}} = 0.012$ (0.779, 60.98%, 85.00%), $\text{ADC} = 0.761 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ (0.781, 93.90%, 55.00%).

Conclusions: QDCE-MRI together with DW-MRI is useful for differentiation between NPC and lymphoma.

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Correspondence to: Mr Xiao-ping Yu. E-mail: nj9015@163.com

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Introduction

In Southeast Asia and China, nasopharyngeal carcinoma (NPC) and lymphoma are two kinds of the most common malignant tumours affecting the nasopharynx. The two tumours differ significantly from each other in terms of their epidemiology, biological behaviour, treatment management and prognosis. Accurate diagnosis is essential to

optimize individual treatment regimens. Currently, non-invasive imaging techniques, particularly MRI and CT, are the main tools used for diagnosing nasopharyngeal tumours; biopsy is also performed, but this method is invasive. Unfortunately, both conventional MRI and CT demonstrate poor diagnostic accuracy in differentiating between lymphoma and NPC, because the two tumours often share similar imaging characteristics on both plain scan and traditional enhancement scan after the intravenous administration of contrast agent.¹ This situation may be attributed to the shortcoming of conventional morphology-based MRI and CT that the two techniques provide little useful functional information about the tumours.

Dynamic contrast-enhanced MRI (DCE-MRI), a functional imaging technique that can reveal the vascularity and perfusion information of tissues, is theoretically expected to be more powerful than traditional MRI in characterizing tumours. Several recent studies^{2,3} have investigated the utility of conventional DCE-MRI for differentiation between certain histological types of tumours in the head and neck, for example, discriminating lymphoma from other malignant tumours. In those studies,^{2,3} the perfusion characteristics of tissues were evaluated according to the model-free semi-quantitative parameters generated from the time–intensity curve (TIC) on conventional DCE-MRI, such as the time to peak enhancement, maximal contrast enhancement and washout ratio. However, the TIC patterns of lymphoma often overlap with those of other malignant tumours such as squamous cell carcinoma and malignant salivary gland tumours,^{2,3} which makes the differential diagnosis based on conventional DCE-MRI quite difficult.^{2,4} This might be, at least in part, attributed to the limitations of the semi-quantitative analysis.⁵ For example, the model-free parameters generated from TIC on DCE-MRI do not directly and accurately reflect the concentration of contrast agent in tissues. In addition, the semi-quantitative parameters may be easily influenced by the MRI settings, imaging protocols and cardiac output of different individuals. These weaknesses limit the clinical application of semi-quantitative DCE-MRI.

Quantitative dynamic contrast-enhanced MRI (QDCE-MRI), a new DCE-MRI method based on pharmacokinetic analysis, has the ability to obtain more direct and specific perfusion information regarding the true vascular physiology, such as microvascular blood flow, vessel permeability and extravascular extracellular space (EES). Therefore, QDCE-MRI has been applied

to characterize the clinical stage, assess the histological grading and aggressiveness and predict the treatment response in a variety of tissues, such as NPC,^{5,6} prostate cancer⁷ and rectal cancer.⁸ Nevertheless, reports on the utility of QDCE-MRI for identifying pathological type of primary tumours are relatively scarce. Several recent studies have manifested the feasibility of QDCE-MRI in differentiation between pancreatic ductal adenocarcinoma and other solid lesions,⁹ between lymphoma and carcinoma in the head and neck¹⁰ and among maxillo-facial tumours.⁶ However, the feasibility of QDCE-MRI for differentiating nasopharyngeal tumours is not clear. Apart from QDCE-MRI, diffusion-weighted MRI (DW-MRI), another functional imaging technique that can measure the mobility of water molecule in tissues, has been used to distinguish NPC from lymphoma. However, conflicting results were reported.^{11,12} Thus, we compared the parameters of both QDCE-MRI and DW-MRI between NPC and lymphoma at the primary site in the present study and evaluated the diagnostic efficacy of these two MRI techniques in the differentiation between the two most common malignancies in nasopharynx.

Methods and materials

Patient selection

This retrospective study was approved by the Medical Ethics Committee of Hunan Cancer Hospital. Data from patients with newly diagnosed, pathologically proven nasopharyngeal lymphoma or NPC Hunan Cancer Hospital from December 2014 to April 2015 were analysed retrospectively. The inclusion criterion was that the patients would have successfully undergone pre-treatment conventional MRI, DW-MRI and QDCE-MRI of nasopharynx. The exclusion criteria included: (1) obvious motion or susceptibility artefacts around the skull base and paranasal sinuses on MRI images, which could prevent the MRI analysis, or (2) difficulty in performing MRI analysis due to small tumour volume (<1 cm³) that led to poor signal-to-noise on MRI images. Initially, 101 patients were recruited. All these patients had been recruited as part of a larger study investigating the utility of DW-MRI and QDCE-MRI in nasopharyngeal tumours and informed consent had been obtained. Of the 123 patients, 21 were eliminated from the study because of serious image distortion (*n* = 7), dental artefacts (*n* = 2) or small tumour volume (*n* = 12). Therefore, 82 patients with NPC (80 non-

Table 1 Comparing the diffusion-weighted MRI and quantitative dynamic contrast-enhanced MRI parameter values between the nasopharyngeal carcinoma (NPC) and lymphoma groups

Groups	n	$K^{trans} (min^{-1})$	$K_{ep} (min^{-1})$	V_e	f_{PV}	$ADC (\times 10^{-3} mm^2 s^{-1})$
Lymphoma	20	0.212 ± 0.059	1.073 ± 0.238	0.213 ± 0.104	0.008 ± 0.007	0.760 ± 0.182
NPC	82	0.366 ± 0.155	1.353 ± 0.468	0.292 ± 0.117	0.027 ± 0.024	0.981 ± 0.184
<i>p</i> -value		<0.001	0.012	<0.001	<0.001	<0.001

ADC, apparent diffusion coefficient; f_{PV} , fractional plasma volume K_{ep} , efflux rate constant; K^{trans} , influx transfer constant; V_e , fractional volume of extravascular extracellular space.

Figure 1 Representative images of nasopharyngeal lymphoma. Images (a–f) are axial T_2 weighted, apparent diffusion coefficient (ADC) K^{trans} , K_{ep} , V_e and f_{PV} maps, respectively. The K^{trans} , K_{ep} , V_e , f_{PV} and ADC values of the tumour were 0.196 min^{-1} , 1.141 min^{-1} , 0.169 , 0.010 and $0.804 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$, respectively.

keratinizing and 2 keratinizing) and 20 patients with lymphoma (15 B-cell non-Hodgkin's and 5 T-cell non-Hodgkin's) were eventually enrolled in the present study. The tumour volumes (mean $\pm$ standard deviation) of lymphoma and NPC were $11.884 \pm 10.610 \text{ cm}^3$ and $10.795 \pm 10.772 \text{ cm}^3$, respectively. For patients with NPC, the distributions of T staging according to the 7th edition of the International Union Against Cancer/American Joint Committee on Cancer (UICC/AJCC) staging system¹³ were as follows: T_1 , $n = 8$ (9.8%); T_2 , $n = 29$ (35.3%); T_3 , $n = 19$ (23.2%); T_4 , $n = 26$ (31.7%).

MRI plain scan protocols

All the MRI examinations were performed on a 1.5-T MRI scanner (Optima[®] MR360; GE Healthcare) with a head and neck coil. The plain scan protocols included: (1) axial T_1 weighted spin echo images [repetition time (TR)/echo time (TE) 580 ms/7.8 ms, 5-mm slice thickness, 1-mm slice gap, slice number 36, number of excitations (NEX) 2]; (2) axial T_2 weighted spin echo images with fat suppression (TR/TE 6289 ms/85 ms, 5-mm section thickness, 1-mm intersection gap, slice number 36, NEX 2); (3) axial DW-MRI with single-shot diffusion-weighted spin echo echoplanar sequence, TR/TE 3870 ms/85.5 ms, 5-mm slice thickness, 1-mm intersection gap, slice number 16, b -values of 0 and 800 s mm^{-2} , matrix 128×128 and NEX 8.

QDCE-MRI and conventional enhanced scan protocols

After the MRI plain scan, multiphase T_1 weighted DCE-MRI images plus pre-contrast T_1 mapping were obtained by using a spoiled gradient echo sequence (liver acquisition with volume acceleration) in the axial plane. Scan parameters were as follows: (1) T_1 mapping: flip

angle 6° , TR 3 ms, TE 1.3 ms, field of view (FOV) 38 cm, slice thickness 5 mm, slice space 1 mm, slice number 16; (2) contrast-enhanced multiphase T_1 weighted MRI acquisition: flip angle 15° , TR 3 ms, TE 1.3 ms, field of view 38 cm, slice thickness 5 mm, slice space 1 mm, slice number 16. Multiphase data sets were acquired every 6 s for 56 times. Intravenous contrast agent injection using a power injector was triggered 15 s after the initial of multiphase MRI data acquisition. Contrast agent gadodiamide (Omniscan[®]; GE Healthcare) was administrated at a dose of 0.1 mmol kg^{-1} of body weight and a ratio of 3.5 ml s^{-1} , followed by a bolus injection of 20-ml normal saline. After finishing acquisition of QDCE-MRI sequences, conventional T_1 weighted contrast scans with fat suppression were performed for staging NPC: (1) axial images: fast spoiled gradient recall acquisition in steady state sequence flip angle 80° , TR/TE 205 ms/2.3 ms, 5-mm slice thickness, 1-mm intersection gap, slice number 36 and NEX; 2 oblique coronal images: (fast spoiled gradient recall acquisition in steady state sequence, flip angle 80° , TR/TE 205 ms/2.5 ms, 5-mm slice thickness, 1-mm intersection gap, slice number 16 and NEX 2).

MRI data analysis

All the MRI data were transferred to an Advantage Workstation with Functool software package (v AW 4.6; GE Medical Systems) for post-processing. The DW-MRI data were fitted to a monoexponential plot to obtain an apparent diffusion coefficient (ADC) map. QDCE-MRI analysis was performed using Cinetool, a software kit for quantitative perfusion evaluation in Functool package. The internal carotid artery was selected to obtain a pooled arterial input function used for the modelling procedure. The following QDEC-MRI

Figure 2 Representative images of nasopharyngeal carcinoma. Images (a–f) are axial T_2 weighted, apparent diffusion coefficient (ADC) K^{trans} , K_{ep} , V_e and f_{PV} maps, respectively. The K^{trans} , K_{ep} , V_e and f_{PV} ADC values of the tumour were 0.389 , 1.532 min^{-1} , 0.328 , 0.021 and $0.932 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$, respectively.

Table 2 Optimal cut-off values of diffusion-weighted MRI and quantitative dynamic contrast-enhanced MRI parameters for the differentiation between nasopharyngeal carcinoma and lymphoma based on receiver operating characteristic curves analysis

Parameters	AUC (95% CI)	Cut-off value	Sensitivity (%)	Specificity (%)	Youden Index
K^{trans}	0.866 (0.794–0.939)	0.262 min ⁻¹	80.49	85.00	0.655
K_{ep}	0.681 (0.569–0.793)	1.401 min ⁻¹	43.90	100.00	0.439
V_e	0.784 (0.648–0.919)	0.211	76.83	85.00	0.618
f_{PV}	0.779 (0.673–0.885)	0.012	60.98	85.00	0.460
ADC	0.781 (0.688–0.857)	0.761×10^{-3} mm ² s ⁻¹	93.90	55.00	0.489

ADC, apparent diffusion coefficient; AUC, area under the curve; CI, confidence interval; f_{PV} , fractional plasma volume K_{ep} , efflux rate constant; K^{trans} , influx transfer constant; V_e , fractional volume of extravascular extracellular space.

parameter maps based on a Tofts and Kermode model analysis¹⁴ were calculated automatically: K^{trans} , K_{ep} , V_e and f_{PV} . K^{trans} is the influx forward volume transfer constant in the EES from the plasma, K_{ep} is the efflux rate constant from the EES to the plasma, V_e indicates the fractional volume of EES per unit volume of tissue ($V_e = K^{trans}/K_{ep}$) and f_{PV} represents the fractional volume of plasma per unit volume of tissue. The DW-MRI and QDCE-MRI metric values for each tumour were independently and double-blindly obtained by two radiologists (WX and FL, with 8 and 10 years' experience in head and neck radiology, respectively) who were blinded to the pathological results. Firstly, the axial image section showing the primary tumour at its widest cross-section was determined on each parameter's map by using T_2 weighted and conventional contrast-enhanced T_1 weighted images as references. Then, three regions of interest (ROIs) were manually drawn by each observer for each tumour at its widest section plus adjacent up and down sections, covering as much of the nasopharyngeal tumour as possible while avoiding the areas of necrosis, air, large vessels and adjacent anatomical structures (*i.e.* fat, muscle and bone). Each metric value was respectively acquired by each observer and correspondingly two initial data points were generated, each of which was the average of the values obtained from the above three ROIs by one observer. The eventual metric value for each tumour was the mean value of the two initial data points.

Statistical analysis

The QDCE-MRI and DW-MRI parameter values for each tumour group were expressed as mean ± standard deviation. The Mann–Whitney *U* test was used to compare these parameter values between the NPC and lymphoma groups. Receiver operating characteristic (ROC) curves were generated with respective cut-off values determined to accommodate best diagnostic accuracy according to the Youden index. All statistical analyses were performed using SPSS® v. 19.0 (IBM Corp., New York, NY; formerly SPSS Inc., Chicago, IL). *p* < 0.05 was considered statistically significant.

Results

The NPC group exhibited significantly higher K^{trans} , K_{ep} , V_e , f_{PV} and ADC values than the lymphoma group

(Table 1). V_e value showed a positive correlation with the ADC value for NPC (*r* = 0.495, *p* < 0.001) and tended to be correlated with the ADC value for lymphoma (*r* = 0.417, *p* = 0.068). Figure 1 and Figure 2 show representative images of NPC and lymphoma, respectively. From the ROC curve analysis, the respective optimal cut-off parameter values (with respective area under the curve (AUC), sensitivity and specificity) are showed in Table 2 and Figure 3.

Discussion

The present study demonstrated that NPC differed significantly from lymphoma in both the ADC value and the QDCE-MRI parameter values, suggesting that QDCE-MRI and DW-MRI may be potentially useful for detecting the tissue characterization of nasopharyngeal tumours and for differentiating NPC from lymphoma.

Up to now, relatively few studies have reported results using quantitative MRI analysis based on

Figure 3 Receiver operating characteristic curves for quantitative dynamic contrast-enhanced MRI diffusion-weighted MRI parameter values with respective areas under the curves. ADC, apparent diffusion coefficient.

pharmacokinetic models to distinguish different nasopharyngeal tumours. Compared with lymphoma, NPC, in this study, presented higher K^{trans} , K_{ep} and f_{PV} values, in accordance with a recent study¹⁰ in which NPC exhibited higher K^{trans} value and an obvious trend of higher f_{PV} value. Meanwhile, semi-quantitative MRI analysis revealed that the area under the contrast concentration curve for both the initial 60 s (IAUC60) and 90 s (IAUC90) were higher for NPC than for lymphoma.¹⁰ On QDCE-MRI, K^{trans} depends on the combination effect of microvascular blood flow, capillary permeability and capillary surface area, whereas K_{ep} is positively correlated only with vessel permeability.¹⁵ Representing the fractional plasma volume of the tissues, f_{PV} is reportedly correlated well with the vascularity (the area of microvessels and blood lakes).¹⁶ Our results and previous observations¹⁰ imply that NPC has more abundant microcirculatory blood flow, vessel surface area, plasma volume and vessel permeability than lymphoma.

As for V_e , its value for NPC was found to be a little higher than that for lymphoma (0.65 ± 0.16 vs 0.54 ± 0.17) in a recent study,¹⁰ but the differences did not approach statistical significance. This difference in the V_e value between the two tumours was verified by our finding that NPC exhibited obviously higher V_e value than lymphoma in the present study. In regard to the difference in the ADC value between NPC and lymphoma, conflicting results^{1,11,12} were reported. In our study, NPC presented significantly higher V_e value than lymphoma, which is in line with the prior studies^{1,11} but disagrees with the finding by Ichikawa *et al*¹² that the two malignancies shared similar ADC value. On QDCE-MRI, V_e is thought to represent the volume of the EES. Compared with lymphoma, NPC exhibited higher V_e value in our study, reflecting that NPC has larger EES. For NPC, this observed larger EES is also suggested by the results of previous studies^{1,11} and the present study that NPC had obviously higher ADC value than lymphoma on DW-MRI. Depending mainly on the cell density and the composition of the extracellular matrix, ADC value is widely believed to be correlated inversely with the tissue cellularity and positively with the volume of EES. This was further intensified by our observations that both significantly positive correlation for NPC and tendency of positive correlation for lymphoma were found between the ADC and V_e values. Thus, the higher ADC value for NPC indicates smaller cellularity and larger EES that is reflected by the higher V_e value. The large EES for NPC may be partly due to necrosis and cystic changes which are believed to be more common in NPC than in lymphoma. Small foci of necrosis and cystic change were

confirmed by pathological examination but were not detected on MRI images in head and neck tumours.¹⁷ On the other hand, compared with NPC, lymphoma is believed to be composed of condensed tumour cells, scarce amounts of stroma and necrosis,^{11,18} which would result in smaller EES and correspondingly lower V_e value.

Among the QDCE-MRI and DW-MRI parameters, K^{trans} had the highest AUC and a relatively high sensitivity in differentiation between the two nasopharyngeal malignancies based on ROC analysis, suggesting that K^{trans} may serve as an important imaging marker for differentiation. K_{ep} had the highest specificity of 100%, whereas its AUC and sensitivity was the lowest, signifying that K_{ep} is a useful marker for differential diagnosis, but its diagnostic efficacy needs to be improved. V_e , f_{PV} and ADC shared moderate AUC in the differentiation, indicating that they have similar feasibility for differentiating NPC from lymphoma.

Our study has several limitations. Firstly, the patient cohort of lymphoma is relatively small. Secondly, we did not correlate the QDCE-MRI and DW-MRI parameters with histological features, such as tumour cell density, nuclear-to-cytoplasm ratio and microvessel density. However, pathological diagnosis of nasopharyngeal tumours is usually based on biopsy specimens that are always small and from the surface of lesions. It is well known that malignant tumour often exhibits histological heterogeneity, namely the surface region of tumour is always associated with more vascularities and less necrosis on microscopic level compared with the central area. Therefore, the pathological features of biopsy specimens may not comprehensively reflect those of the entire tumour. Thirdly, the MRI analysis in this study was based on drawing an ROI covering the entire solid parenchyma of tumours to survey the mean value. This does not adequately reflect the heterogeneity of tumours such as NPC. Although the information gathered from the entire tumour might be more readily applicable to tumour evaluation,^{19,20} further studies that utilize regional hot-spot analysis, pixel-by-pixel analysis or liquefactive necrosis portion analysis may be more meaningful in comprehensively characterizing different nasopharyngeal tumours.

Conclusions

In conclusion, this study shows that NPC exhibits different perfusion and diffusion MRI characteristics from lymphoma. QDCE-MRI together with DW-MRI is potentially useful for the differentiation between the two nasopharyngeal tumours, which is often a clinical diagnostic dilemma.

References

1. Kato H, Kanematsu M, Kawaguchi S, Watanabe H, Mizuta K, Aoki M. Evaluation of imaging findings differentiating extranodal non-Hodgkin's lymphoma from squamous cell carcinoma in naso- and oropharynx. *Clin Imaging* 2013; **37**: 657–63. doi: <http://dx.doi.org/10.1016/j.clinimag.2012.11.007>
2. Matsuzaki H, Hara M, Yanagi Y, Asami J, Katase N, Unetsubo T, *et al*. Magnetic resonance imaging (MRI) and dynamic MRI

- evaluation of extranodal non-Hodgkin lymphoma in oral and maxillofacial regions. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2012; **113**: 126–33. doi: <http://dx.doi.org/10.1016/j.tripleo.2011.07.038>
3. Sumi M, Nakamura T. Head and neck tumours: combined MRI assessment based on IVIM and TIC analyses for the differentiation of tumors of different histological types. *Eur Radiol* 2014; **24**: 223–31. doi: <http://dx.doi.org/10.1007/s00330-013-3002-z>
 4. Kitamoto E, Chikui T, Kawano S, Ohga M, Kobayashi K, Matsuo Y, et al. The application of dynamic contrast-enhanced MRI and diffusion-weighted MRI in patients with maxillofacial tumors. *Acad Radiol* 2015; **22**: 210–16. doi: <http://dx.doi.org/10.1016/j.acra.2014.08.016>
 5. Huang B, Wong CS, Whitcher B, Kwong DL, Lai V, Chan Q, et al. Dynamic contrast-enhanced magnetic resonance imaging for characterising nasopharyngeal carcinoma: comparison of semi-quantitative and quantitative parameters and correlation with tumour stage. *Eur Radiol* 2013; **23**: 1495–502. doi: <http://dx.doi.org/10.1007/s00330-012-2740-7>
 6. Zheng D, Chen Y, Liu X, Chen Y, Xu L, Ren W, et al. Early response to chemoradiotherapy for nasopharyngeal carcinoma treatment: value of dynamic contrast-enhanced 3.0 T MRI. *J Magn Reson Imaging* 2015; **41**: 1528–40. doi: <http://dx.doi.org/10.1002/jmri.24723>
 7. Vos EK, Litjens GJ, Kobus T, Hambroek T, Hulsbergen-van de Kaa CA, Barentsz JO, et al. Assessment of prostate cancer aggressiveness using dynamic contrast-enhanced magnetic resonance imaging at 3 T. *Eur Urol* 2013; **64**: 448–55. doi: <http://dx.doi.org/10.1016/j.eururo.2013.05.045>
 8. Yao WW, Zhang H, Ding B, Fu T, Jia H, Pang L, et al. Rectal cancer: 3D dynamic contrast-enhanced MRI; correlation with microvascular density and clinicopathological features. *Radiol Med* 2011; **116**: 366–74. doi: <http://dx.doi.org/10.1007/s11547-011-0628-2>
 9. Liu K, Xie P, Peng W, Zhou Z. Assessment of dynamic contrast-enhanced magnetic resonance imaging in the differentiation of pancreatic ductal adenocarcinoma from other pancreatic solid lesions. *Comput Assist Tomogr* 2014; **38**: 681–6. doi: <http://dx.doi.org/10.1097/RCT.0000000000000120>
 10. Lee FK, King AD, Ma BB, Yeung DK. Dynamic contrast enhancement magnetic resonance imaging (DCE-MRI) for differential diagnosis in head and neck cancers. *Eur J Radiol* 2012; **81**: 784–8. doi: <http://dx.doi.org/10.1016/j.ejrad.2011.01.089>
 11. Fong D, Bhatia KS, Yeung D, King AD. Diagnostic accuracy of diffusion-weighted MR imaging for nasopharyngeal carcinoma, head and neck lymphoma and squamous cell carcinoma at the primary site. *Oral Oncol* 2010; **46**: 603–06. doi: <http://dx.doi.org/10.1016/j.oraloncology.2010.05.004>
 12. Ichikawa Y, Sumi M, Sasaki M, Sumi T, Nakamura T. Efficacy of diffusion-weighted imaging for the differentiation between lymphomas and carcinomas of the nasopharynx and oropharynx: correlations of apparent diffusion coefficients and histologic features. *AJNR Am J Neuroradiol* 2012; **33**: 761–6. doi: <http://dx.doi.org/10.3174/ajnr.A2834>
 13. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. *Ann Surg Oncol* 2010; **17**: 1471–4. doi: <http://dx.doi.org/10.1245/s10434-010-0985-4>
 14. Tofts PS. Modeling tracer kinetics in dynamic Gd-DTPA MR imaging. *J Magn Reson Imaging* 1997; **7**: 91–101. doi: <http://dx.doi.org/10.1002/jmri.1880070113>
 15. Yi B, Kang DK, Yoon D, Jung YS, Kim KS, Yim H, et al. Is there any correlation between model-based perfusion parameters and model-free parameters of time-signal intensity curve on dynamic contrast enhanced MRI in breast cancer patients? *Eur Radiol* 2014; **24**: 1089–96. doi: <http://dx.doi.org/10.1007/s00330-014-3100-6>
 16. Sennino B, Raatschen HJ, Wendland MF, Fu Y, You WK, Shames DM, et al. Correlative dynamic contrast MRI and microscopic assessments of tumor vascularity in RIP-Tag2 transgenic mice. *Magn Reson Med* 2009; **62**: 616–25. doi: <http://dx.doi.org/10.1002/mrm.22040>
 17. Wang J, Takashima S, Takayama F, Kawakami S, Saito A, Matsushita T, et al. Head and neck lesions: characterization with diffusion-weighted echo-planar MR imaging. *Radiology* 2001; **220**: 621–30. doi: <http://dx.doi.org/10.1148/radiol.2202010063>
 18. Sumi M, Nakamura T. Head and neck tumors: assessment of perfusion-related parameters and diffusion coefficients based on the intravoxel incoherent motion model. *AJNR Am J Neuroradiol* 2013; **34**: 410–16. doi: <http://dx.doi.org/10.3174/ajnr.A3227>
 19. Ungersma SE, Pacheco G, Ho C, Yee SF, Ross J, van Bruggen N, et al. Vessel imaging with viable tumor analysis for quantification of tumor angiogenesis. *Magn Reson Med* 2010; **63**: 1637–47. doi: <http://dx.doi.org/10.1002/mrm.22442>
 20. Kim JH, Im GH, Yang J, Choi D, Lee WJ, Lee JH. Quantitative dynamic contrast-enhanced MRI for mouse models using automatic detection of the arterial input function. *NMR Biomed* 2012; **25**: 674–84. doi: <http://dx.doi.org/10.1002/nbm.1784>