Lymph node volume and apparent diffusion coefficient as a biomarker for metastatic invasion in an experimental model

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Background

Lymph node metastasis is an important prognostic factor for patients diagnosed with cancer. It determines choice of adjuvant treatment and is strongly correlated with survival rates in many different malignancies. Nodal staging often requires surgical removal and histopathological analysis of regional lymph node bearing tissue. This procedure is invasive, expensive and is associated with complications and morbidity. The most commonly used MR criterion for determining nodal invasion is lymph node size, as estimated by the short or long axis diameter exceeding 10mm. This criterion is specific, however not very sensitive to metastatic nodes. An estimated 50-80% of lymphatic metastases in gynaecological malignancies measure less than 10mm in shortest diameter and are therefore not identified as metastatic[1,2]. Diffusion Weighted Imaging is an imaging method which evaluates tissue based on Brownian motion of water protons. Metastatic invasion may induce changes in the diffusion characteristics of tissue, amongst others by increasing cellularity. These changes can be quantified as changes in the apparent diffusion coefficient (ADC).

Objective

This abstract describes an experimental lymph node metastasis model in which metastatic popliteal lymph nodes are followed over time using MRI. To predict metastatic invasion, two parameters are serially studied: 1) lymph node volume and 2) mean lymph node ADC.

Methods

Imaging: Eight Copenhagen rats were scanned on a 3.0T MR scanner using an 8 channel human wrist coil. Imaging started 1 day prior to tumour cell implantation and was repeated two days later, and from then on every three days until 14 days after cell implantation. The imaging protocol consisted of: axial and coronal T2-weighted datasets, a coronal T1-weighted data set, and a diffusion weighted scan with b-values: 0, and 1000 s/mm^2 (see Figure 1).

Tumour cell implantation: After the baseline measurements of both popliteal lymph nodes, R3327 MAT LyLu prostate tumour cells were injected in the right hind footpad. The animals were divided into 2 groups of 4 rats each, receiving a suspension of either 40,000 or 250,000 tumour cells. The animals were checked daily for clinical as well as behavioural parameters. When the volume of the metastatic node exceeded 25 mm^3, the animals were sacrificed.

Image analysis: All images were analyzed using in-house software by a experienced reviewer with knowledge of the model. Volumes were calculated by drawing regions of interest (ROIs) around the lymph nodes and by subsequently integrating the ROIs over all slices. Volume analysis was done on the axial T2-weighted images, as well as on the coronal T1- and T2-weighted images. For the ADC measurement, ROIs were drawn in the b=0 diffusion weighted image and copied to the corresponding ADC map (see Fig 1C).

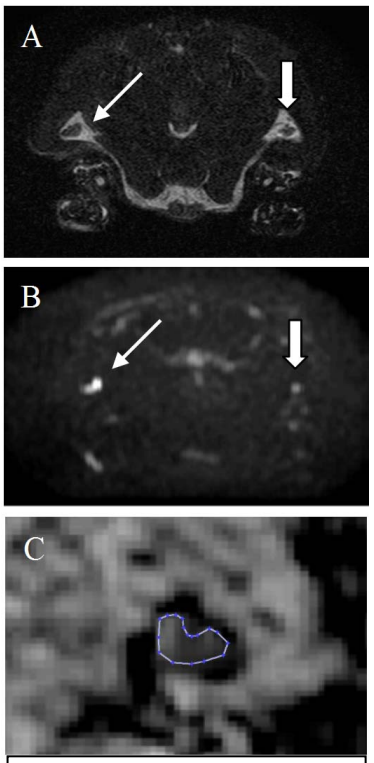


Figure 1: **A.** axial T2-weighted image showing the contralateral control lymph node (thin arrow) and the metastatic popliteal lymph node (fat arrow).
B. Corresponding diffusion-weighted image (b=1000).
C. Corresponding ADC map zoomed in on metastatic lymph node, showing example ROI for ADC measurement.

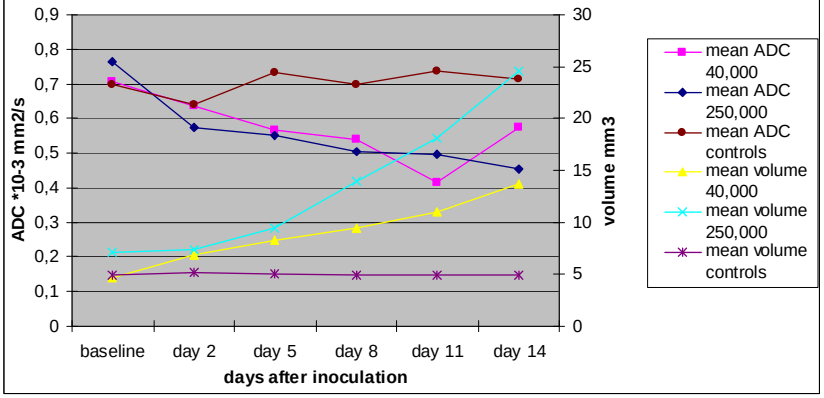
Results:

1. Volume: when the two groups of tumour draining nodes combined were compared to the contralateral healthy control nodes, nodal volumes differed significantly starting from 5 days after inoculation (oneway ANOVA, p=0.006). All three groups differed significant significantly from each in terms of volume increase starting at 8 days after tumour cell implantation.
2. ADC: already on day 2, with minimal lymph node volume increase, the ADC in metastatic nodes started to decrease compared to the baseline ADC in these nodes. The differences in ADC between metastatic and healthy control nodes became significant 8 days after tumour cell implantation (p=0.002, Figure 2).

Conclusion/ Discussion:

A straightforward and reproducible model of lymph node metastasis was developed that allowed serial imaging analysis over time. A decrease in ADC of metastatic lymph nodes was found simultaneously with volume changes in that node suggesting that ADC might be used as a biomarker predicting tumour implantation and lymph node growth.

Figure 2: ADC and volume of metastastic nodes over time



References:

1) Benedetti et al. Gynecol Oncol 1999;62:19-24.
2) Tangjitgamol et al. Int J Gynecol.Cancer 2006;16:1880-4.