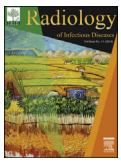
HOSTED BY

ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

Radiology of Infectious Diseases 1 (2014) 17−21



www.elsevier.com/locate/jrid

Research article

Noninvasive assessment of perfusion in virus-associated VX2 tumors using MR spin labeling technique

Renhua Wu [a,c,*], David F. Kallmes [b,c]

[a] Department of Radiology, The 2nd Affiliated Hospital, Shantou University Medical College, Shantou 515041, China
[b] Department of Radiology, Mayo Clinic, 200 First St SW, Rochester, MN 55905, USA
[c] Department of Radiology, University of Virginia Health Services, Charlottesville, VA 22908, USA

Received 20 August 2014; accepted 18 October 2014
Available online 8 November 2014

Abstract

The purpose of this study was to evaluate an MR arterial spin-labeling technique to characterize regions of hyper- and hypovascularity in virus-associated rabbit VX2 tumors. Shope papillomavirus-associated VX2 carcinoma cells were implanted bilaterally in the thigh musculature of 17 New Zealand White rabbits. MR imaging sequences included a T2-weighted sequence and the arterial spin-labeling technique, flow-sensitive alternating inversion recovery with an extra radiofrequency pulse (FAIRER). Areas of viable and non-viable tumor were estimated based on the spin echo imaging sequences. Perfusion images were obtained from a magnitude subtraction of the labeled from the unlabeled images from the FAIRER sequence. Region of interest (ROI) analysis was performed in muscle, viable tumor regions, and necrotic tumor regions. Mean ROI signal intensities for viable tumor vs. muscle and necrotic tumor vs. muscle were compared using the student *t*-test. Spin echo imaging demonstrated tumors in 30 of 34 thighs. Perfusion images were successfully obtained in all cases. Mean ROIs were significantly greater in regions of viable tumor compared to those in muscle ($p < 0.001$). Mean ROIs were significantly less in regions of necrotic tumor compared to those in muscle ($p < 0.001$). Virus-associated VX2 tumors serve a good model for evaluating arterial spin labeling technique. This technique may be valuable in diagnosing hypervascular areas of tumors that would be amenable to preoperative embolization, such as intracranial meningiomas.

Keywords: Shope papillomavirus; VX2 tumor; Magnetic resonance imaging; Perfusion; Arterial spin labeling

1. Introduction

Measurement of tissue perfusion provides important information about tissue hemodynamics under normal and pathological conditions. Organ viability and function can be depicted by in vivo measurement of perfusion. Tissue perfusion imaging can be performed with many techniques, including single photon emission computed tomography and positron emission tomography. These nuclear medicine modalities, while valuable, suffer from low temporal and spatial resolution and involve ionizing radiation. Magnetic resonance imaging (MRI) allows high resolution imaging, and both anatomic and functional assessments can be obtained during the same imaging session. Recently, a significant amount of interest has been shown in using MRI to measure tissue perfusion.

A number of MRI methods have been described for the measurement of tissue perfusion. First-pass MR imaging after injection of intravascular contrast agents [1−3] has been used extensively. However, venous access and bolus injection devices are necessary for the first-pass method. More recently, arterial spin labeling techniques [4−14], such as EPISTAR (Echo Planar Imaging and Signal Targeting with Alternating Radiofrequency), FAIR (Flow-sensitive Alternating Inversion

* Corresponding author. Department of Radiology, The Second Affiliated Hospital, Shantou University Medical College, Dong Sha Bei Lu, Shantou 515041, China. Tel./fax: +86 754 88915674.
E-mail address: rhwu@stu.edu.cn (R. Wu).
Peer review under responsibility of Beijing You'an Hospital affiliated to Capital Medical University.

http://dx.doi.org/10.1016/j.jrid.2014.10.006

Recovery), and other variants, have been developed in an effort to measure tissue perfusion noninvasively.

The arterial spin-labeling technique has been applied in measuring brain perfusion [15–18], cardiac perfusion [19], and renal perfusion [20,21]. This technique has not been widely applied to the study of vascular tumors. In many centers, preoperative embolization of intracranial meningiomas is performed routinely to limit intraoperative blood loss and allow optimal tumor resection. Meningiomas may be avascular in a significant minority of cases, but the extent of tumor vascularity usually is defined only at the time of the conventional angiogram. A reliable, noninvasive perfusion technique would allow more efficient preoperative evaluation of patients with meningioma, since those patients with avascular tumors could avoid the need for conventional angiography.

The purpose of this study was to evaluate the feasibility of using an arterial spin-labeling technique, Flow-sensitive Alternating Inversion Recovery with an Extra Radiofrequency pulse (FAIRER), to identify hyper- and hypovascular areas of tumor in an experimental rabbit model of Shope papillomavirus-associated VX2 tumors.

2. Materials and methods

2.1. Animal models and preparation

All animal procedures were approved by the Animal Research Committee at the institution. The Shope papillomavirus-associated VX2 tumor is a malignant tumor found in New Zealand White rabbits, and has served as an established model of vascular tumors in rabbits. Seventeen adult New Zealand White rabbits (3–5 kg) bearing VX2 tumors were included in this study. The VX2 tumor was prepared according to previously reported method [22,23]. Shope papillomavirus-associated VX2 carcinoma cells were implanted bilaterally in the thighs of the rabbits. MRI was performed 14–28 days following inoculation of tumor cells. Tumor size at the time of imaging was typically 1–4 cm diameter. Prior to the MRI examination, the rabbits were intramuscularly anesthetized with 6 mg/kg ketamine and 6 mg/kg xylazine, and maintained under anesthesia with periodic intravenous injection of 0.6 mg/kg ketamine.

2.2. MRI examination

All rabbits were examined with a 1.5-T whole-body scanner (Magnetom Vision, Siemens, Iselin, NJ) at room temperature. An extremity coil was used. All rabbits were scanned in the supine position. After obtaining a scout image, T2-weighted images (turbo spin echo sequence, TR/TE = 4000/99, field of view 230 mm, slice thickness 8 mm, matrix 256 × 256, 1 average) were obtained for tumor detection. The perfusion imaging slices were chosen by reference to T2-weighted images.

2.3. Perfusion imaging (FAIRER sequence)

The details of the FAIRER technique have been described elsewhere [12,24]. Briefly, a preparatory inversion pulse was applied, followed immediately by a selective 90° radiofrequency pulse centered on the imaging plane, followed by dephasing gradients. The control image was obtained using a spatially selective inversion pulse, and the tag image using a nonselective inversion pulse. Subtracting the tag image from the control image produced the perfusion-weighted image. A centric reordered TurboFLASH sequence was used. The sequence parameters were: flip angle = 12°, TR/TE = 4.6 msec/2.0 msec, FOV = 230 mm, slice thickness 8 mm, matrix 256 × 256, total scan duration 1 min 47 s per slice. Ten acquisitions were averaged. The time delay, TD, between image acquisition was 4s to allow magnetization recovery of the tissue and tagged blood. TD is the time between the end of one image acquisition and the beginning of the next tagging period. Three adjacent slices of tumor were scanned with FAIRER sequence. A magnitude subtraction of the control from the tag images was performed on console.

2.4. Data analysis

We had previously noted on histologic evaluation that most tumors of greater than 3 cm diameter contained both viable tumor, usually present along the periphery, as well as necrotic areas, usually within the central aspect of the tumors (unpublished data). In many cases the perfusion image demonstrated areas of increased signal peripherally, which we denoted as “tumor” for analytic purposes. Conversely, in many cases the perfusion image demonstrated areas of diminished signal intensity centrally, which we denoted as “necrosis” for analytic purposes. Identical slices of perfusion image and T2-weighted image were compared. ROI analysis was performed by selecting areas of muscle, tumor, and necrosis based on the T2-weighted imaging sequence. The muscle region was either selected in adductor magnus muscle or in vastus lateralis muscle depending on the location without tumor involvement. The ROIs were outlined using an interactive computer display. Each ROI contained at least 10 pixels on perfusion image. The carefully shaped ROI had an arbitrary, irregular contour to match the shape of tumor, necrosis and muscle [3,25].

To compare perfusion in VX2 tumors, mean and standard deviation of “tumor,” “necrosis,” and muscle were calculated. Ratio of tumor/muscle and ratio of necrosis/muscle were also calculated. Because some data were not applicable, the unpaired student *t*-test was used for determining the significance of difference between the means.

3. Results

Thirty of 34 thighs contained tumors visible on spin echo imaging. Perfusion images were successfully obtained in both thighs of all 17 rabbits. Examples are shown in Figs. 1 and 2. The signal intensity changes in tumor and necrotic component are shown in Tables 1 and 2.

The results of signal intensity (gray scale) measured in muscle and viable tumor are shown in Table 1. The mean of signal intensity in muscle was 5.0 ± 0.8. The means of signal intensity in tumor were 11.7 ± 3.9 (left side) and 11.0 ± 3.1