Initial experiences with Flat-Panel-Volume Computed Tomography (VCT) for imaging tumour angiogenesis in nude mice: Comparison with micro MR-angiography

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Synopsis

The Volume Computed Tomograph (VCT) is the prototype of a new CT-scanner developed by General Electrics using flat panel detectors for high resolution three dimensional (3D) imaging. Purpose of this study was to investigate, whether high resolution contrast enhanced micro-angiography can be performed in tumour bearing nude mice using this new technology. Additionally, the quality of VCT-angiography images was assessed by comparison with MR-angiography at 1.5T and immuno-histological images (CD31 vessel stain) of excised tumours.

Methods

The scan protocol for VCT-angiography was optimised using 12 nude mice with subcutaneous squamous cell carcinomas. Three contrast agents and different injection volumes were tested: Iopramid 300 (300mg I/ml), Iomeprol 400 (400mg I/ml) and bariumsulfate (50mg/ml). Scan parameters were varied between 50-100kV and 40-200mAs. Contrast agent was injected manually with 30 seconds injection time 20 seconds before the scan. The whole mouse was captured in two rotations with 4 seconds scan time/rotation and isotropic voxels of $(50\mu m)^3$. Scan quality was assessed in a multi-reader analysis by scoring imaging quality of large arteries and veins, cerebral vessels, draining tumour vessels, small vessels inside the tumours and homogeneity of contrast inside the vessels.

In a second experiment VCT- and the corresponding MR-angiographies of 6 tumour bearing mice were compared. Contrast enhanced MR-angiography (contrast media: Gadomer 17, Schering, Berlin, Germany; 0.1mmol Gd/kg body weight) was performed on a 1.5T whole body MR scanner (Symphony, Siemens, Erlangen, Germany) using a custom built animal coil for excitation and reception [1]. A high resolution FLASH 3D sequence (TR/TE=13.3/6.2 ms, flipp-angle=50º, BW=150 Hz/pixel, NEX=1) was applied before and immediately after intravenous injection of contrast media as described previously [2]. The next day animals were examined with VCT angiography twice, first using Iomeprol 400 and 90 minutes later using Bariumsulfate (50mg/ml). After the bariumsulfate enhanced scan, animals were sacrificed in deep anaesthesia. Tumours were removed, sectioned and a CD31/Keratin double immunofluorescence stain of vessels and tumours cells was performed on histological slices.

Results

VCT displayed detailed vessel-architecture of mice and tumours (figure 1). Best VCT scan quality was reached with bariumsulfate, which is however, lethal for the animals when injected intraveneously. Contrast enhanced scans using 500µl Iopramid were of comparable quality and were tolerated by the animals without complications. On 3D-reconstructions draining tumour vessels were tracked from their outlet. Large vessels infiltrating the tumour showed enlarged diameter and a contorted curse, which is typical for malignant angio-achitecture. Furthermore, diffuse networks of small vessels inside the tumours indicated malignant tissue. Discrimination of vital and necrotic regions was improved by analysing local heterogeneity of vascularisation. Larger vessels highly matched on images of VCT, MRI and histology. However, small vessels inside the tumours, which branch from infiltrating vessel threads were visualised by VCT to a higher degree than by MRI (figure 2) due to its the higher spatial resolution and better vessel contrast. The measurement of vessel diameters on VCT, MRI and immunofluorescence images (CD31 vessel stain) indicated that vessels down to 200µm diameter were imaged with MRI, while VCT was capable to visualise even smaller vessels with less than 100µm diameter.

Discussion

We were able to show for the first time that VCT is a excellent tool to visualise micro-vessels in tumours. At this, presentation of vessel-architecture in VCT scans was more detailed as in the contrast enhanced MR-angiography at 1.5 Tesla. Other non-invasive modalities such as micro CT have also shown potential to image micro-vessels of excised tumours [3]. However, shorter scan times of the VCT improve its usability for experimental in vivo studies and the larger diameter of the gantry suggests its application in clinical research.

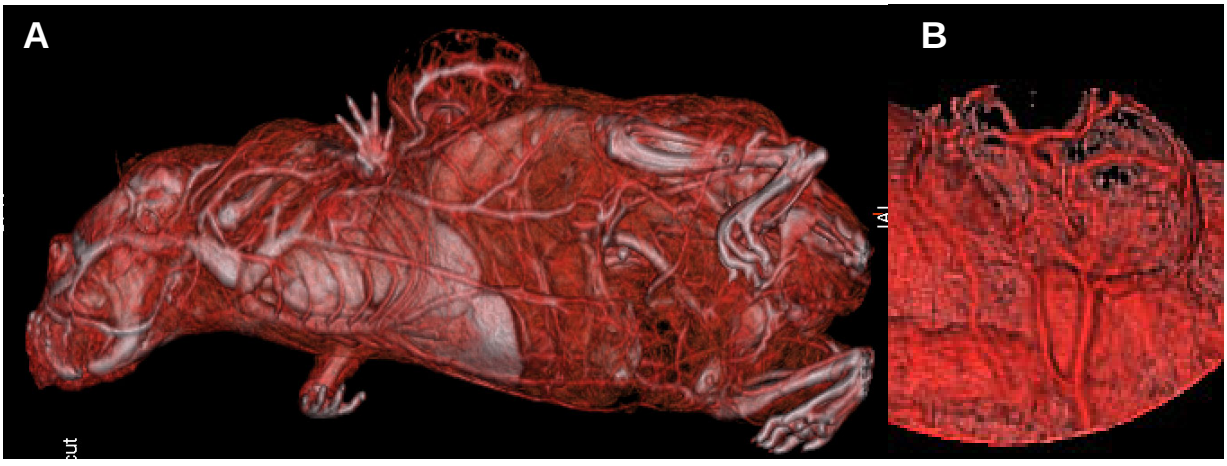

Figure 1: The 3D-VCT image of a tumour bearing nude mouse (A) and the magnification of the tumour (B) shows dilatated feeding vessels with contourted curse infiltrating the tumour and building a diffuse network, which is typical for malignant tissue.

References

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