Occlusion of blood flow by high intensity focused ultrasound

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Abstract: Blood flow occlusion in vivo using a single high intensity focused ultrasound exposure is investigated. A high power 1.7 MHz, 150 mm focal length, piezoelectric ultrasound transducer was used to expose femoral vessels to free field spatial peak intensities in the range 750-4660 Wcm⁻² whilst being moved at constant speed. Pre- and post-FUS exposure, sub-millimetre resolution magnetic resonance datasets were acquired using a Siemens Vision System (1.5T), with and without contrast agent administration. The minimum dose for reliable occlusion was 1200 Wcm⁻². We believe this effect can be exploited to treat conditions where alternative invasive treatments have high associated risks of mortality and morbidity.

INTRODUCTION

Focused ultrasound surgery (FUS) has been used since the 1940’s to create soft tissue damage at depth, via heating and/or cavitation, without damage to overlying tissues(1). FUS has been applied as a non-invasive treatment for a variety of conditions(2) especially in neurology(3), oncology(4), ophthalmology(5) and urology(6). Both tissue sparing around large blood vessels(7,8,9) and the perfusion independence of FUS lesion size for exposures less than 2 seconds in duration(8,10) are well documented. Vascular occlusion has been studied using 7 MHz FUS, at a spatial peak intensity (Iₚ) of 167 Wcm⁻² for 3 seconds to induce thrombosis in veins(11), and using 1.5 MHz FUS to occlude rabbit renal arteries up to 0.7 mm in diameter under magnetic resonance image (MRI) guidance using an array of exposures at two power levels (6500 Wcm⁻² for and 2800 Wcm⁻² for 10s) to show vessel blockage and infarction damage in the kidney up to 7 days after FUS(12). More recently, we have shown an occluding effect of FUS at 1.7 MHz using an array of exposures 2 mm apart at a single free field Iₚ level of 4660 Wcm⁻² (13). The study described below determines a minimum ‘single shot’ intensity capable of producing reliable occlusion.

METHODS

The FUS system uses a focused bowl piezoelectric ceramic (PZT4) crystal, with a radius of curvature of 15 cm and diameter of 10 cm, operated at 1.69 MHz(4). All free field Iₚ values were determined to within 10% using a radiation force balance and hydrophone measured beam profiles(14). The transducer was attached to a gantry which allowed full 3D positioning(4), and was located using a mechanical pointer such that the focal peak lay 5mm beneath the tissue surface in order to minimise the risk of radiation pressure rupture of the exposed vessel walls. A stepper motor was used to move the gantry supporting the transducer at constant speed. Vascular occlusion was studied in rat (n=9) femoral vessels in accordance with Home Office regulations. Non-recovery animals were anaesthetised using an intraperitoneal injection of hypnorm and hypnovel for up to 2 hours. A skin incision was made to remove the highly absorbing skin from the FUS path, and to allow visualisation of the vessels for targeting. Both rear limbs were submerged in a tank of degassed water (~25°C) to ensure that a cone shaped water bath attached to the transducer was in good acoustic contact with the target(13). This arrangement avoided applying pressure to the femoral vessels during exposure. By varying the intensity from 750 to 4660 Wcm⁻², the minimum Iₚ required to produce reliable occlusion in vivo using a continuous 5s exposure during which the transducer was moved at 1.0 mms⁻¹ orthogonally across the femoral vessels was investigated using MR methods.

MR images were obtained using a Siemens Vision MR System (1.5T) and a Siemens extremity coil. FISP-3D magnitude contrast angiograms (TR=50ms, TE=14ms, Fl=15°, FOV=100x200mm, Ma=128x256, NEX=2) with an in-plane spatial resolution of 0.78x0.78mm and 1.0mm slice thickness were used to measure signals arising only from flowing blood. Fat suppressed FLASH-3D images (TR=33.8ms, TE=5ms, Fl=20°, FOV=100x200mm, Ma=128x256, NEX=2) with the same resolution were also acquired, and a fat suppressed DESS sequence (TR=44ms, TE=9ms, Fl=70°, FOV=100x200mm, Ma=128x256, NEX=1) of the same resolution was used to study both blood flow and tissue damage using a single sequence. Images were obtained before and after FUS exposure.
Post FUS MR data were obtained before and after intravenous injection of 0.05 mmol/kg of the blood pool contrast agent polylysine-Gd-DTPA (Schering AG, Berlin). Vascular patency was assessed clinically by visual examination of the vessels, and using the MR images to compare FUS exposed limbs with the appearance of both the pretreatment thigh and the contra-lateral thigh. Occlusion was demonstrated by a lack of flow in the MRA (FISP) images, and a signal void in the treated region shown by contrast enhanced 3D FLASH and DESS images and when (post- minus pre-contrast) subtraction FLASH and DESS datasets were obtained. Maximum intensity projection (MIP) post processing gave 2D representations of the full 3D datasets for analysis and presentation.

RESULTS

Figure 6 in the plenary lecture paper by G.R. ter Haar in this volume demonstrates a typical study in which the post-ultrasound MR angiogram (MRA) shows no blood flow in the exposed thigh compared with both the pre-ultrasound MRA and the contralateral (unexposed) thigh. Figure 1 shows the effects on occlusion of exposures at various intensities. Starting from a level (4660 Wcm⁻²) known to produce occlusion, the intensity was reduced until no occlusion was obtained at 750 Wcm⁻². The intensity was then increased until occlusion was reliably obtained in 3/3 studies at 1220 Wcm⁻².

CONCLUSIONS & DISCUSSION

This study demonstrates our ability to occlude rat femoral vessels in vivo with a single intensity 1.7 MHz FUS exposure during which the transducer was moved at a constant speed of 1.0mm/s. This is an extension of a pilot study(13) which demonstrated FUS occlusion and the suitability of MR imaging (with and without contrast agent) for its assessment. Recent studies showing a single placental vessel ~3 mm in diameter to be responsible for the abnormal blood flow which causes FFTS(15) lead us to be optimistic that diagnostic ultrasound guided FUS may offer a non-invasive treatment, probably without the need for anaesthetic. This study was supported by the MRC, CRC, Wiseman Trust and Schering AG, Berlin.

REFERENCES