High-resolution ex vivo magnetic resonance angiography: a feasibility study on biological and medical tissues

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Introduction: In biomedical science *in vivo* angiography is frequently employed to produce a structural overview of the intravascular configuration in living tissues, whereas *ex vivo* angiographies of excised organs and post-mortem angiographies are rarely performed. However, *ex vivo* angiography can be a practical and valuable mean to elucidate vascular structures three-dimensionally with simultaneous determination of intravascular volume and hereby provide information secondary to conventional autopsy. The aim of this study was to develop novel contrast agents and methods for *ex vivo* angiography using both magnetic resonance angiography (MRA) and computed tomography angiography (CTA) and demonstrate and compare the usefulness of these methods in elucidating vascular structures in four different organs and species: the human placenta, the rice field eel, the porcine heart and the red-eared slider (turtle).

Materials and methods: The experimental study was conducted in several steps. Prior to MRA and CTA of selected specimens, we defined the optimal concentration of contrast agent for MRA using test tubes containing different concentrations of gadoteric acid (0-4 mmol/L) until maximum signal intensity was obtained. Next, the effect of formalin on permeability of blood vessel walls was elucidated aided by Scanning Electron Microscopy (CamScan MaXim 2040 EnVac SEM). Two solutions with contrast agents were prepared, one agent containing a saline solution of gelatin (0.05 g/mL), the CT contrast agent barium sulphate (0.1 g/mL) and the MR contrast agent gadoteric acid (2.5 mmol/L), the other solution containing a saline solution of albumin (60 g/L) and the albumin-binding MR contrast agent gadofosveset trisodium (2.5 mmol/L). Subseque0ntly, samples of four different species and organs, the human placenta, the rice field eel, porcine heart and the turtle, were perfused with the contrast solutions and subjected to MRA and CTA protocols using a GE Horizon Echospeed LX 1.5 T for MRA and a Siemens Somatom Definition with dual source capacity for CTA. The MRA sequence was based on a standard clinical 3D T1-weighted gradient-echo technique. Data acquired by MRA and CTA were exported to DICOM format and 3D reconstruction was performed using either Mistar (www.apollomit.com) or Osirix (http://www.osirix-viewer.com) software. The ability of MRA and CTA to elucidate vessel structure in the four species and organs was determined and compared.

Results and Discussion: Our study showed that MRA could only be performed on fresh tissue since formalin fixation makes the blood vessels permeable to the MR contrast agent due to the presence of microscopic holes in the vessel wall following formalin fixation (fig. 1). Both solutions proved useful, and it was possible to perform *ex vivo* angiography on all specimens (fig. 2-5). Fig. 2 presents a MRA and a CTA of a human placenta perfused with gadoteric acid based contrast agent. The vessel structure of minor vessels is clearly more visible in the MRA. Fig. 3 shows a MRA and CTA of a rice field eel. CTA suffers from the presence of adjacent bones to the blood vessels that interfere with the signal from blood vessels. Fig. 4 presents a MRA and CTA of the coronary arteries in the same porcine heart. Again MRA is capable of elucidating minor vessel structures more clearly. Fig. 5 shows a MRA and CTA of the heart and associated blood vessels in a red-eared slider, where both MRA and CTA are capable of elucidating major vessels, whereas minor vessels are seen more clearly in the MRA. Of the two solutions prepared the gadofosveset trisodium based contrast agent was superior when only MRA was performed, whereas the gadoteric acid and barium sulphate based agent was more useful in situations where both MRA and CTA were performed.

Conclusion: We found that MRA provided detailed information similar to or better than conventional CTA. Especially, MRA has a great advantage over CTA in its ability to visualize only the vessel configuration without interfering signals from adjacent bones as seen in CTA. The two solutions used in this study are relatively easy to prepare and can both be used for *ex vivo* MRA, and the barium sulphate containing solution can be used for CTA in addition.

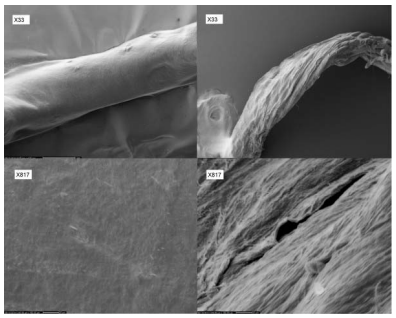

Fig. 1. Left: SEM of fresh blood vessel in placenta. No holes in vessel wall. **Right**: SEM of formalin-fixed blood vessel in placenta. Note holes in vessel wall.

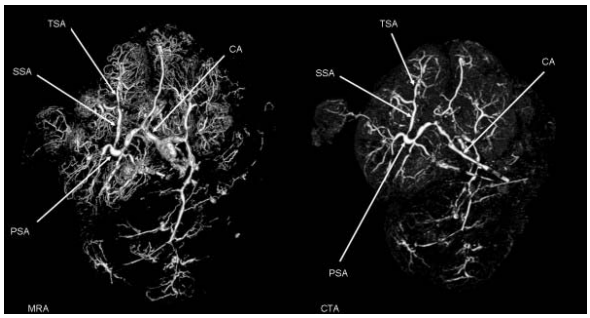

Fig. 2. Left: MRA of human placenta. **Right**: CTA of human placenta. Key: CA, chorionic artery; PSA, primary stem artery; SSA, secondary stem artery; TSA, tertiary stem artery.

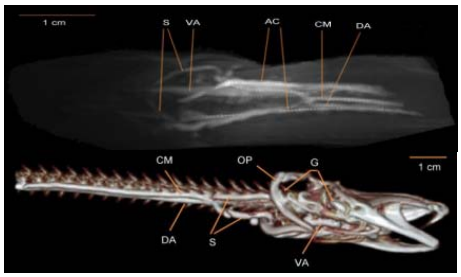

Fig. 3. MRA (top) and CTA (bottom) of gill region of a rice field eel. Key: VA, ventral aorta; DA, dorsal aorta; S,shunt vessel; CM, celiacomesenteric artery; AC, anterior cardinal veins.

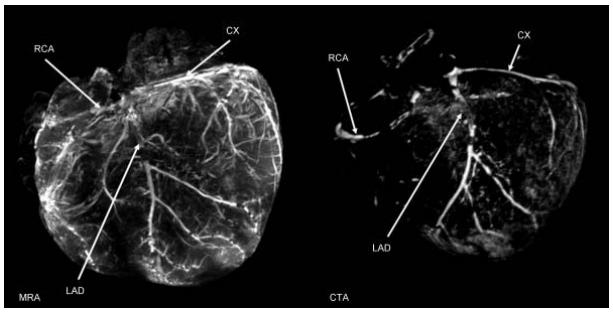

Fig. 4. MRA (left) and CTA (right) of the same porcine heart. Key: LAD, left anterior descending artery; CX, circumflex artery; RCA, right coronary artery.

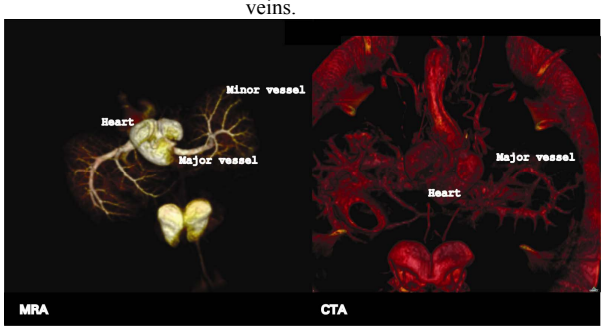

Fig. 5. MRA (left) and CTA (right) of the heart and associated blood vessels in a red-eared slider.