Background: Allogeneic mesenchymal stem cells (MSCs) offer an alternative therapy to induce arteriogenesis for peripheral artery disease (PAD) patients who are not candidates for conventional surgical or medical therapies. However, current methods lack the ability to non-invasively monitor cell delivery, engraftment, and therapeutic benefit. The purpose of our study was to validate non-invasive in vivo tracking of MSCs using alginate-poly-L-lysine-alginate (APA) microcapsules containing perfluorooctylbromide (PFOB) with c-arm CT and 19F MRI.

Methods: New Zealand White rabbits (n=16) received 6 injections of PFOB microcapsules in the medial thigh. C-arm CT (0.31x0.31x0.31 mm voxel size) and 19F MR (1.25x1.25x2 mm voxel size) images were acquired 1-14 days post treatment. Rabbits were humanely sacrificed and perfusion fixed prior to sectioning the medial thigh into 2.5 mm transverse sections, which were digitally imaged. Injections sites were contoured manually on the digital images.

MR and post-mortem digital images were rendered as 3D volumes and co-registered with CT volumes using custom software (Dextroscope). Registration offsets were calculated as the linear distance between paired CT and postmortem injection sites or paired MRI and CT injection sites.

Results: A high percentage of the injection sites were identified and visualized on CT (94.8% of 96), MRI (95.8% of 24) and post-mortem images (95.6% of 96). Registration offsets were 2.83 ± 0.85 mm between paired CT/post-mortem injection sites and 0.32 ± 0.14 mm between paired MRI/CT injection sites.

Conclusions: The high correlation between the spatial locations of CT, MRI, and postmortem injection sites indicates that the radiopacities on CT and hotspots on MRI accurately depict the PFOB capsule locations. The offsets of MRI/CT registration were small despite the lower spatial resolution of MRI relative to CT whereas the potential displacement in positioning due to tissue fixation and sectioning resulted in a larger offset between the post-mortem/CT registration. Thus, PFOB impregnated APA microcapsules offer the first reliable method for tracking MSC injection sites for cardiovascular therapy in vivo by both c-arm CT and 19F MRI.