

MRI-Monitored IntraTIPS Local Delivery of Motexafin Gadolinium: Towards Improving Long-Term Patency of TIPS

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Introduction:

Transjugular intrahepatic portosystemic shunt (TIPS) has become an important and effective interventional procedure in treatment of the complications related to portal hypertension. Although the primary patency of TIPS has been greatly improved due to the recent clinical application of cover stent-grafts, the long-term patency of TIPS is still dismal. In this study, we attempted to develop a new technique of MRI-guided intraTIPS local agent delivery, which aimed to ultimately inhibit shuntstenosis and facilitate the bridging of those patients to liver transplantations.

Materials and Methods:

Six domestic pigs underwent TIPS procedure in an angiography suite. Before placement of the stent, a custom-made microporous delivery balloon catheter was placed into the shunt, and the pig was then transferred to a 3T MR scanner. Via the microporous balloon, 15-mL Motexafin gadolinium (MGd, 75 µg/mL, Pharmacyclics Inc.) mixed with trypan blue dye was locally delivered into the shunt-hepatic vein wall under dynamic MRI monitoring. Before and after MGd/blue mixture delivery, T1-weighted MR images of the shunt-vein wall were taken. The contrast-to-noise ratios (CNR) of pre- and post-MGd/blue delivery MRI were then measured and compared. After MRI, an 8-mm stent was deployed through the shunt in the angiography suite. After completion of the procedure, the stented shunt along with the hepatic and portal vein segments was harvested and cross-sectioned at 5-µm thickness. The section slides were then stained with H&E for anatomic confirmation, as well as examined with fluorescent microscopy for detection of delivered red-fluoresce-emitting MGd and light microscopy for visualization of delivered blue dye within the shunt-vein wall.

Results:

TIPS procedures were technically successful in all six pigs. Dynamic MRI displayed in-shunt MGd/blue penetration into the shunt-vein walls. Post-delivery MRI showed the enhancement of the shunt-vein walls in comparison to pre-delivery MRI (Figure A to D). Analysis of MR signal intensities demonstrated higher average CNR on post-delivery MRI than that on pre-delivery MRI (60.5±12.4 vs 13.8±2.6). The MRI manifestations correlated well with subsequent histological examination, showing penetrated MGd as red-fluorescent spots and blue-dye infiltration through the shunt - hepatic vein walls (Figure E to J).

Conclusion:

MRI-monitored intraTIPS local agent delivery is feasible in an animal model, which may open new avenues to improve the long-term patency of TIPS by using MRI-guided drug/gene therapy to limit in-TIPS stenosis and thrombosis, as well as facilitate bridging of those patients to liver transplantations.

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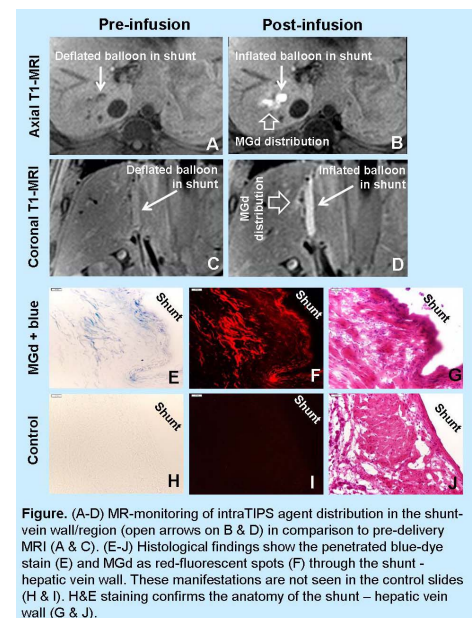


Figure. (A-D) MR-monitoring of intraTIPS agent distribution in the shunt-vein wall/region (open arrows on B & D) in comparison to pre-delivery MRI (A & C). (E-J) Histological findings show the penetrated blue-dye stain (E) and MGd as red-fluorescent spots (F) through the shunt - hepatic vein wall. These manifestations are not seen in the control slides (H & I). H&E staining confirms the anatomy of the shunt - hepatic vein wall (G & J).