USE OF MRI IN THE ANALYSIS OF CORPORAL FIBROSIS IN THE RAT.

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Introduction

Recent reports have revealed that sildenafil may aid in the preservation of erectile function following radical prostatectomy (RP) [1]. However, there has not yet been a non-invasive method of detecting fibrotic changes in the penis following neural injury, which frequently occurs during RP. This series of experiments was undertaken to develop a protocol for the imaging of the rat corpora cavernosum using MRI in the setting of cavernous nerve injury [2]. Additionally, sildenafil was used so that its ability to abrogate the cascade of fibrotic events could be ascertained [3].

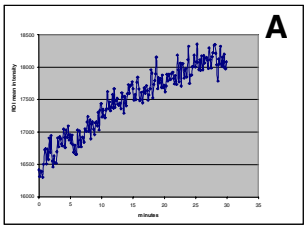
Methods

Three-month-old male Sprague-Dawley rats were divided into 5 groups comprised of 3 animals each. CONTROL: no cavernous nerve (CN) crush, no sildenafil. CN-7d: 7 day s/p CN crush, no sildenafil. CN-7d-V: 7 day s/p CN crush, 20 mg/kg sildenafil daily. CN-28d-V: 28 day s/p CN crush, no sildenafil. CN-28d-V: 28 day s/p CN crush, 20 mg/kg sildenafil daily. All treated animals received the last dose of sildenafil 24 hours prior to MR imaging and sacrifice surgery. All animals underwent non-contrast penile MRI with and without intracavernosal injection of 5 mg of papaverine. One animal from each group underwent gadolinium enhanced penile MRI with and without papaverine induced erection. At the completion of scanning, animals were sacrificed, penises were harvested and whole-mount corporal bodies were evaluated with Masson's Trichrome (MT). Image analysis software was used to quantify MT staining (Image J, NIH).

All MR scans were performed on a Bruker Biospec 4.7T spectrometer (Bruker Biospin MRI, Billerica, MA) with a home-built 5-turn solenoid coil (ID 7 mm, length 2 cm). Rats were placed in the prone position with the penis positioned in the solenoid coil with suture. Three-dimensional anatomical images were acquired using a 3D RARE sequence with TR=1s, TE=55 ms, RARE factor=8, with a spatial resolution of 94 x 104 x 104 µm. For Dynamic Contrast-Enhanced (DCE) MRI, Gd-DTPA (0.2 mmol/kg) was injected via tail vein and a series of 6 T1-weighted axial slices (1 mm thickness) were acquired. The spatial resolution was 104 x 104 µm, dynamic time resolution, 11 s. Images were processed off-line using AFNI (Medical College of Wisconsin, Milwaukee, WI) and IDL (ITT Visual Information Solutions, Boulder, CO) software suites.

Results and Discussion

There was no difference in corporal cavernosal (CC) volume between pre- and post-papaverine injection. The average signal intensity (Gd enhancement) for the CC decreased after injection ($p<0.05$). This drop in intensity is most likely due to penile arterial in-flow. The dynamic enhanced images of CC showed alteration of enhancement pattern after CN crush. For normal rat penis the enhancement was slow in the flaccid state but there was a rapid enhancement phase and a slow wash-out during erection (Fig.1). Seven days post CN crush, the CC enhancement patterns for flaccid and erect state were reversed (Fig. 2). Twenty-eight days post CN crush with daily sildenafil treatment, enhancement patterns were similar to control (Fig. 3), indicating the restorative or protective effect of sildenafil. Masson's trichrome staining of whole-mounted penises revealed significant preservation of smooth muscle in the sildenafil treated groups vs. non-treated groups (CONTROL=43%, CN-7d=18.5%, CN-7d-V=40%, CN-28d=17.0%, CN-28d-V=46%; $p<0.005$).



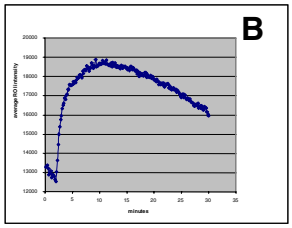
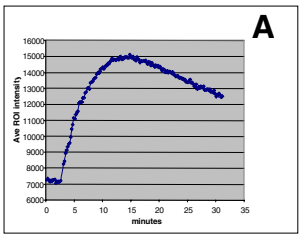


Figure 1



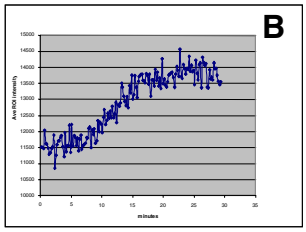
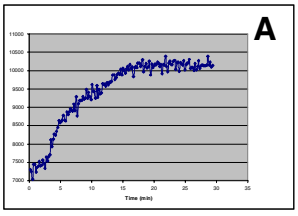


Figure 2



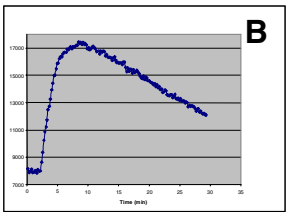


Figure 3

Conclusion

These results suggest that the use of penile MRI is an excellent modality for non-invasive imaging of corporal fibrosis in the cavernous nerve injury rat model. The utilization of this modality has far-reaching implications for the management of patients undergoing radical pelvic surgery.

References

1) Mulhall, J. et. al, J Sex Med. 2005, 2:104-108. 2) Kaneko, K. et. al, Radiology, 1994, 191:75-77. 3) Ferrini, M. et. al, J. Urol., 2006, 68:429-435.