MR MICRO-NEUROGRAPHY IN THE INVESTIGATION OF AMYLOID-RELATED NEUROPATHY

Paolo F Felisaz¹, Eric Y Chang², Polesel Marco¹, Irene Carne³, Maugeri Giulia¹, Giovanni Palladini⁴, Obici Laura⁴, Giampaolo Merlini⁴, Baldi Maurizia⁵, Stefano Bastianello⁶, and Fabrizio Calliada¹

¹Radiology Department, University of Pavia, Pavia, Italy, ²Radiology Service, VA San Diego Healthcare System, San Diego, CA, United States, ³Medical Physics Department, IRCCS Salvatore Maugeri Foundation, Scientific Institute of Pavia, Italy, ⁴Amyloid Research and Treatment Center, Scientific Institute Policlinico San Matteo, Pavia, Italy, ⁵Radiology Department, IRCCS Salvatore Maugeri Foundation, Scientific Institute of Pavia, Italy, ⁶Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy

<u>TARGET AUDIENCE</u> people interested in amyloid-related neuropathy and high resolution MRI. <u>INTRODUCTION</u>

Peripheral neuropathy (PN) can be associated with systemic amyloidosis, typically starting in the lower limbs with proximal progression. The two most common amyloid-related neuropathies are caused by light chain (AL) and mutated-TTR. Early diagnosis may impact patient outcome since the treatment may stop, or even reverse, the progression of the disease¹. Diagnosis of PN is based on electrophysiology and clinical evaluation, but MRI may play an important role^{2,3}. MR micro-neurography allows evaluation of peripheral nerves below 100 µm resolution, with demonstration of tissue detail at a level comparable with light microscopy after histologic staining. In this study, we evaluated patients with various grades of amyloid-related neuropathy of the lower limbs, utilizing a clinical MRI scanner with readily available sequences and coils.

MATERIALS AND METHODS

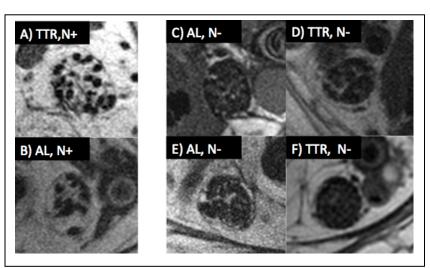
6 patients affected by amyloid neuropathy (3 AL and 3 mutated-TTR) were investigated at the level of the ankle to obtain MR microscopic images of the posterior tibial nerve. Age of the patients ranged from 32 to 73 years old. Imaging was performed on a Discovery MR750 3T scanner (GE Healthcare, USA) using a 6-Channel Carotid Array Coil, adapted for the investigation of the ankle region. High resolution sequences were acquired with the following parameters. 3D spoiled gradient echo with chemical fat suppression with TR 16 ms, TE 6 ms, flip angle 10°, matrix size 512 x 420, FOV of 5 cm, slice thickness 62 mm for a coverage of 2 cm, bandwidth 25 kHz, NEX 5, time of scan approx. 10-12 min. 2D TSE T1-w with TR 650ms, TE 25ms, ETL 5, Matrix size 512 x 512, FOV of 5 cm, slice thickness 2 mm with 0.5 mm gap, bandwidth 30 kHz, NEX 6, time of scan approx. 8-10 min.

RESULTS

Typical MR micro-neurograms demonstrated the various components of the nerve such as the paraneural fascia, the epineurium, the epineurial fat, the nerve fascicles and even the perineurium (Fig. 1). Different patterns of micro-neurography in patients with severe and mild PN are shown in Fig. 2. Nerves in patients with severe PN (PND stage ≥III) demonstrate a reduced number of fascicles surrounded by epineurial fat in relative larger amount than in mild ones. Nerves of patients affected by mild PN present a reduced amount of epineurial fat with a preserved number of fascicles.

DISCUSSION

MR micro-neurography has the capability of detailing amyloid-related nerve pathology to a much greater degree compared with conventional MR- neurographic techniques^{2,3}. Microscopic components of nerves may be seen using a clinical 3T scanner with readily available coils and sequences. We have shown that PNs in patients with amyloid neuropathy demonstrate an obvious pathologic pattern with increased amounts of fat and decreased number of fascicles. MR micro-neurography may potentially be a valuable tool for the post-treatment follow-up of patients with AL and TTR related neuropathy as well as for detecting the initial stage of these neuropathies.



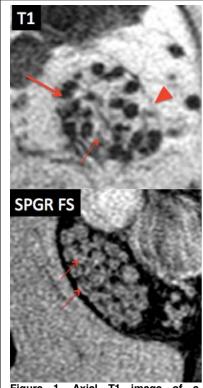


Figure 1. Axial T1 image of a pathologic nerve. Big arrow = fascicle; arrowhead = paraneural fascia; small arrow = epineurium and fibrous tissue. Epineurial fat is seen between the fascicles, in larger amount than in normal nerves. Fibrous epineurium between the fascicles is seen. FS SPGR - normal nerve. The fascicles are seen in a dark background (fat suppressed + fibrous epineurium). The perineurium surrounding the single fascicles is also seen with higher signal (arrow).

REFERENCES

1. Palladini G, Eur J Intern Med 2013 Dec;24(8):729-39. 2. Kollmer J, MR-neurography: In-vivo detection of nerve injury in systemic light chain (AL) amyloidosis, presented at ISA, Indianapolis, 2014. 3. Kollmer J, Early in-vivo detection of lower limb nerve injury in hereditary transthyretin familial amyloid polyneuropathy using high-resolution MR-neurography, presented at ISA, Indianapolis, 2014

Figure 2 Posterior tibial nerves, axial section at the ankle. 2D TSE T1 weighted. AL / TTR = type of amyloidosis; N+ = severe PN with motor impairment; N- = mild PN, mainly sensitive. In severe neuropathy there is a larger amount of inter-fascicular fat and a reduced number of fascicles compared with mild neuropathy.