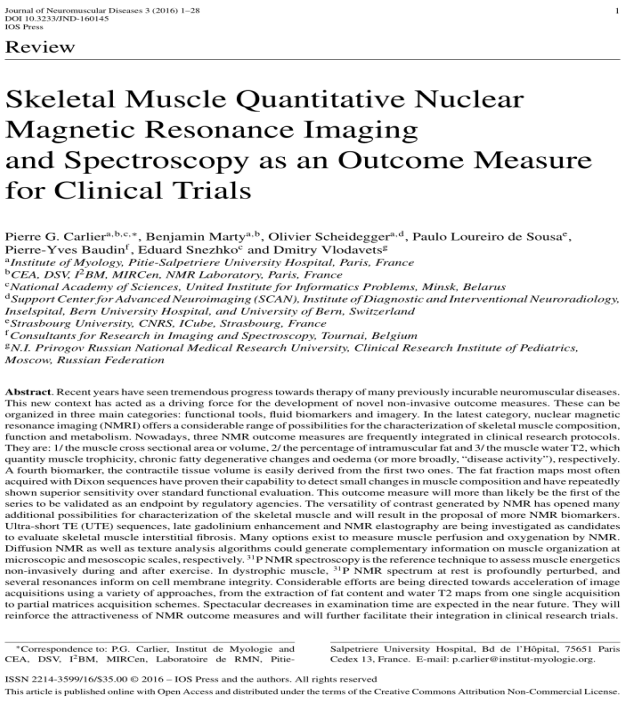
Diseases Of Muscle: Pathological Foundations Of Clinical Myology



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Review

Skeletal Muscle Quantitative Nuclear Magnetic Resonance Imaging and Spectroscopy as an Outcome Measure for Clinical Trials

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Abstract. Recent years have seen tremendous progress towards therapy of many previously incurable neuromuscular diseases. This new context has acted as a driving force for the development of novel non-invasive outcome measures. These can be organized in three main categories: functional tools, fluid biomarkers and imagery. In the latest category, nuclear magnetic resonance imaging (NMRI) offers a considerable range of possibilities for the characterization of skeletal muscle composition, function and metabolism. Nowadays, three NMR outcome measures are frequently integrated in clinical research protocols. They are: 1/ the muscle cross sectional area or volume, 2/ the percentage of intramuscular fat and 3/ the muscle water T2, which quantity muscle trophicity, chronic fatty degenerative changes and oedema (or more broadly, "disease activity"), respectively. A fourth biomarker, the contractile tissue volume is easily derived from the first two ones. The fat fraction maps most often acquired with Dixon sequences have proven their capability to detect small changes in muscle composition and have repeatedly shown superior sensitivity over standard functional evaluation. This outcome measure will more than likely be the first of the series to be validated as an endpoint by regulatory agencies. The versatility of contrast generated by NMR has opened many additional possibilities for characterization of the skeletal muscle and will result in the proposal of more NMR biomarkers. Ultra-short TE (UTE) sequences, late gadolinium enhancement and NMR elastography are being investigated as candidates to evaluate skeletal muscle interstitial fibrosis. Many options exist to measure muscle perfusion and oxygenation by NMR. Diffusion NMR as well as texture analysis algorithms could generate complementary information on muscle organization at microscopic and mesoscopic scales, respectively. ^{31}P NMR spectroscopy is the reference technique to assess muscle energetics non-invasively during and after exercise. In dystrophic muscle, ^{31}P NMR spectrum at rest is profoundly perturbed, and several resonances inform on cell membrane integrity. Considerable efforts are being directed towards acceleration of image acquisitions using a variety of approaches, from the extraction of fat content and water T2 maps from one single acquisition to partial matrices acquisition schemes. Spectacular decreases in examination time are expected in the near future. They will reinforce the attractiveness of NMR outcome measures and will further facilitate their integration in clinical research trials.

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