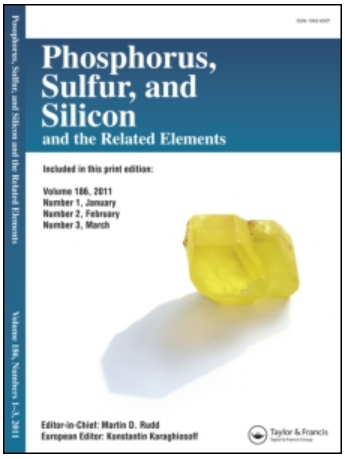

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Medical Applications of ^{31}P Nuclear Magnetic Resonance

Joachim Seelig[a]
[a] Biocenter of the University of Basel, Switzerland

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MEDICAL APPLICATIONS OF ^{31}P NUCLEAR MAGNETIC RESONANCE

JOACHIM SEELIG
Biocenter of the University of Basel, Switzerland

Abstract ^{31}P NMR can be applied to study the metabolism in vivo in animals and humans. The most important phosphate metabolites are ATP, phosphocreatine, and inorganic phosphate. From the chemical shift of the inorganic phosphate resonance it is possible to measure the internal pH. ^{31}P-NMR is applied to occlusive arterial desease of the legs, to bone tumors, and to study effects of the anti-cancer drug adriamycin on the energy metabolism of in vivo rat heart.

INTRODUCTION

Over the past 15 years ^{31}P NMR spectroscopy has been developed into a valuable tool for the non-invasive study of phosphorus containing metabolites in in vivo studies. In 1973 Moon and Richards discovered that the chemical shift of the inorganic phosphate resonance could be calibrated to measure the internal pH in red blood cells and in other tissues [1]. Shortly thereafter, the potential of ^{31}P NMR for the non-invasive assessment of energy metabolism was fully appreciated [2]. The technique has been used for the determination of phosphorus metabolites (phosphocreatine PCr, adenosinetriphosphate ATP, inorganic phosphate P_i) in hereditary and acquired disorders of muscle metabolism [3-6]. Investigations using ^{31}P NMR demonstrated that forearm exercise in healthy subjects resulted in PCr depletion and intercellular acidosis [7-9].

CLINICAL APPLICATIONS

The energy metabolism of calf muscle was assessed by ^{31}P NMR in eleven patients with symptomatic arterial occlusions [10]. Foot exercise was performed in the magnet while blood flow in the leg

was shortly interrupted by applying a tourniquet. During ischemic exercise PCr decreased from its resting concentration of 20 mM to undetectable levels whereas P_i increased concomitantly. After removal of the cuff, PCr recovery followed a single exponential but the recovery showed significant differences between patients and controls. PCr recovery was characterized by a half-time of 200 ± 70 s in patients compared to 37 ± 5 s in controls. Intracellular pH recovered more slowly in patients than in controls. Half-time of P_i disappearance after removal of the tourniquet was similar in magnitude as PCr recovery, confirming the intimate biochemical connection of the two metabolites.

High resolution ^{31}P NMR spectra were also obtained of four patients with bone tumors of their distal extremities [11]. In one case the tumor was investigated during clinical remission after radiation therapy and chemotherapy. The other three cases showed clinically active tumor growth with correspondingly increased metabolism. The spectra of the three active tumors indicated a relatively high ATP concentration, similar to previously published spectra from animal tumors or human tumors implanted into animals. The P_i resonance also showed strong signal intensity while the PCr resonance was rather weak. Additional resonances were observed in the phosphomonoester and phosphodiester region. These metabolites are usually not seen in healthy muscle tissue.

The antibiotic adriamycin (ADM) is active against a wide variety of human and experimental tumors. The major side-effect of clinical relevance is the development of a cumulative, dose-dependent cardiotoxicity. ADM appears to interfere drastically with the oxidative phosphorylation in the heart mitochondria. In vivo ^{31}P NMR was therefore used to measure the effects of ADM on the energy metabolism of the rat heart [12]. The exclusive acquisition of NMR signal from cardiac muscle was assured by positioning a solenoidal radiofrequency NMR coil around the heart

Administration of ADM led to an immediate decline in the cardiac levels of PCr and stabilization at a new, lower steady state level occurred. Longer term effects of single high doses and of multiple lower doses were measured up to a week after initiation of the treatment. It appeared that drug induced interference with cardiac energy metabolism at the same total dose was more pronounced in the acute phase and markedly increased at longer times.

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