Article published online: 2026-01-12

Beyond Protons (1H1): The Era of Multinuclear Magnetic Resonance Imaging

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Indian J Radiol Imaging

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Sir,

Since its inception, clinical magnetic resonance imaging (MRI) has almost exclusively relied on proton (^{1}H) signal acquisition, owing to the high natural abundance and sensitivity of hydrogen in biological tissues. However, other nuclei—collectively termed X-nuclei—possess unique biochemical and physiologic signatures that can be directly interrogated by MRI, providing information inaccessible to conventional proton-based sequences. Recent technological advances in hardware, pulse sequence design, and hyperpolarization techniques are catalyzing the transition of multinuclear MRI from a research tool to targeted clinical applications.

Technical Foundations

Many X-nuclei, including ^{23}Na, ^{31}P, ^{19}F, ^{17}O, ^{7}Li, ^{39}K, and ^{35}Cl, have lower gyromagnetic ratios and natural abundances than ^{1}H, resulting in reduced signal-to-noise ratio (SNR) and often rapid relaxation. Optimized ultrashort echo time (UTE) and non-Cartesian k-space sampling schemes (e.g., 3D radial, cones) help capture short-T2 signals, while high-field systems ($\geq$7 T) and dual-tuned or broadband radiofrequency coils improve sensitivity. Hyperpolarization techniques—spin-exchange optical pumping for ^{129}Xe and dissolution dynamic nuclear polarization for ^{13}C—boost signal by several orders of magnitude, enabling real-time metabolic imaging.

Select Clinical Applications

^{23}Na MRI quantifies tissue sodium concentration, offering insight into cellular viability, cartilage glycosaminoglycan depletion, and renal corticomedullary gradients.[1] ^{31}P spectroscopy measures high-energy phosphate metabolism and intracellular pH, aiding in the evaluation of cardiomyopathies and neuromuscular disorders.[2] Hyperpolarized ^{13}C MRI, particularly using [1-^{13}C]pyruvate, visualizes dynamic metabolic fluxes and has shown promise for early treatment-response assessment in brain and prostate tumors.[3]

Hyperpolarized ^{129}Xe MRI—recently cleared by the US FDA for ventilation imaging—maps pulmonary ventilation, alveolar–capillary barrier uptake, and red blood cell transfer, facilitating the assessment of asthma, chronic obstructive pulmonary disease, and interstitial lung disease.[4,5] ^{19}F MRI provides background-free "hot-spot" imaging for cell tracking and inflammation mapping, while ^{17}O MRI allows direct measurement of cerebral oxygen consumption. ^{7}Li MRI has demonstrated the ability to map in vivo brain lithium distribution, potentially guiding therapy in bipolar disorder.

Future Directions

The coming years are likely to see broader clinical adoption in three main areas:

1. **Pulmonology:** Regional ventilation and gas-exchange mapping with ^{129}Xe.
2. **Oncology:** Hyperpolarized ^{13}C for metabolic characterization and early therapy response.
3. **Nephrology:** ^{23}Na mapping for functional assessment before structural changes occur.

Integration with routine ^{1}H imaging, vendor-neutral reconstruction pipelines, and standardized quantification protocols will be critical for multicenter reproducibility. Expansion of

DOI https://doi.org/10.1055/s-0045-1814136.
ISSN 0971-3026.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

hyperpolarized agent portfolios and modular upgrades for existing scanners could make multinuclear imaging more accessible.

Conclusion

Multinuclear MRI extends the diagnostic potential of MRI by providing direct, noninvasive access to tissue biochemistry and physiology. Continued technical refinement, growing clinical evidence, and regulatory milestones position these techniques as key enablers of precision imaging in the next decade.

Note

Multinuclear MRI is transitioning from niche research to clinically impactful imaging, offering unique physiologic and metabolic insights that complement conventional proton MRI in precision medicine.

Conflict of Interest

None declared.

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