# Physician's Expectations for Human UHF

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The challenge for clinical translation of new technology is to distill novel ideas into practice. For ultra-high field (UHF) MRI researchers, this means thinking not just about a scientific question or challenge, but also about how any new understanding can be transformed into an advantage in medical care.

This involves thinking first about *unmet need*: what are relevant medical needs that are not well addressed now? Having identified a need, what would doctors would recognise from the new technology as better meeting the need?

In general, doctors are looking for more confident diagnoses and more efficient management of patients. However, development of a new medical technology also needs to take into account the concerns of patients and payers. Patients are look to medical technologies for earlier detection and diagnosis so that the morbidity is reduced, lower uncertainty and faster and more effective initiation of any necessary treatment, all done in ways that are more comfortable or more convenient. Payers attend to the "bottom line": lower costs and improved health outcomes.

Creating a "vision" for a new technology in the future medical arena is a useful exercise even as the underpinning science is being explored. This can help to prioritise the choice of potential application areas for exploration and help to define the most important scientific questions that need to be addressed. It also can help set the high goals that must be achieved. For example, precisely what health outcomes are most meaningful? What would need to be done to show an improvement over standard of care? This demands thinking not just about the biomedical science, but also how the resulting technology would be incorporated into current models for medical care to improve practice outcomes and reduce costs.

What doctors, patients and payers join in looking for with any new technology are high value applications, validations of utility and a clear path to cost effective delivery. These issues incidentally are typically also central to thinking by research funders.

Clinical applications of 7T MRI (or higher field strengths) still are very limited, but there are promising opportunities already apparent for neurosurgical applications. For example, smaller cerebral cavernous malformations and the anatomy of associated venous malformations, can be better defined using 7T than 3T MRI[1]. Does this greater sensitivity mean that treatment outcomes can be improved? 7T susceptibility weighted imaging may better characterize the intratumoral vascular architecture and microstructure of brain gliomas in ways that may yield a useful biomarker of tumor grade[2]. Could this reduce the numbers of biopsies that need to be performed for tumour grading? Functional neurosurgical targeting may also be made more precise. UHF contrast and resolution

enhance the segmentation of the sub-thalamic nucleus and have provided evidence for a lateral shift with aging[3]. The feasibility of using 7 T MR images of the central brain regions for functional neurosurgical targeting structures such as the STN has been demonstrated[4]. Would incorporation of this information enhance the quality of deep brain stimulation outcomes? Approaches to evaluations for new neurosurgical technologies are well established. These examples provide good reason to hope that specialized neurosurgical centres could better meet their objectives with UHF MRI.

There are several applications with more limited direct clinical application that may be able to provide a case for clinical value of UHF MRI. For example, cortical inflammatory lesions in patients with multiple sclerosis may be better visualized and sub-types discriminated at 7T. A recent study has demonstrated that leukocortical (type I) and subpial (III-IV) are potential cortical biomarkers of cognitive and neurologic status in MS[5]. In patients with Alzheimer's disease, CA1 pyramidal apical dendrite loss provides a measure of some of the earliest neuropathology and selective CA1 atrophy assessed with high resolution UHF MRI correlates well with memory functions, suggesting its potential for risk stratification or monitoring of treatment outcomes[6]. Signal hyper intensity in the cervical lateral corticospinal tract in motor neuron disease patients may provide a biomarker of the relevant pathology[7] and loss of lateral edge of the substantia nigra and changes in especially more rostrally could allow direct monitoring of neurodegeneration in Parkinson's disease[8]. The increased sensitivity of UKF MRI for MR spectroscopic imaging could enable improved focal localization of MRSI abnormalities to identify an area for resection, although clinical evidence that it would improve health outcomes likely would be difficult to generate[9].

It still is very early in the development of 7T MRI technology. Fundamental technical challenges of UHF are slowly being resolved, e.g., reducing susceptibility distortions to allow imaging near air cavities[10]. Improved acquisition methods also should allow more rapid high resolution imaging [11]. Integration of conventional structural measures with advanced approaches to tractography should allow improvements in the discrimination of cytoarchitectonically distinct grey matter regions[12], potentially offering additional opportunities and safer functional neurosurgery. Contrast mechanisms specific to UHF MRI, such as those from magnetic anisotropy of white matter[8], or those that are enhanced in UHF, such as iron content imaging[13], may make new kinds of assessments of brain injury possible. Integration of UHF MRI with PET molecular imaging could enhance specificity of interpretation of molecular metabolic signals[14].

As a field, we are just starting to explore clinical applications. We should approach this exploration with a sense of optimism. In this brief overview, the real promise has been highlighted for making use of the improvements in sensitivity for localized spectroscopy and for high resolution neuropathological anatomy imaging and the field strength dependence for exploitation of novel contrast mechanisms. There are several promising niche neurosurgical applications for tumour grading, localization of ictal foci in epilepsy and evaluation of subcortical nuclear structure for functional neurosurgery. Growing interest in pre-symptomatic or early diagnosis of Alzheimer's disease could provide a larger potential population for high-resolution hippocampal imaging (or related) as disease modifying therapies become available.

The former applications could justify routine use for some applications at specialized care centres and the latter, were such structural markers shown to be better predictive of outcome and cost effective relative to alternatives (e.g., clinical measures, lower field MRI or PET), could bring expansion to a wider marker. Researchers seriously interested in translational UHF applications should consider not only the scientific advantages of a method, but how it would be validated, demonstrated to lead to superior outcomes relative to the current standard of practice and be able to be deployed in a cost effective fashion. Also, what adjunct technologies (such as image analysis computational algorithms) need to be developed robustly to make the concept translationally viable? This kind of thinking demands input from a wide community, including medical physics, radiology and the neuroscience specialties, patients, payers and manufacturers of imaging systems. To best realize benefits to patients of this promising, but high cost platform technology, the research community should attend explicitly to creating the kinds of partnerships needed for this.

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