**Resting Functional Connectivity: Potential as a Clinical Marker in Individual Patients**

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**Twenty years after the discovery of fMRI, the clinical applications of this promising approach remain severely restricted. A handful of neurosurgical centers routinely use fMRI for functional localization in pre-surgical mapping. Beyond this basic application, fMRI has thus far failed to live up to its clinical potential. The lack of applications is due in large part to the poor signal to noise ratio of fMRI, but also relates to the difficulty of using task-based fMRI in clinical setting and clinical populations. Task-presentation and response recording devices are cumbersome to operate and maintain in standard clinical settings. Further, it is difficult for patients with prominent neurologic or psychiatric symptoms to perform tasks accurately (or at all) in the scanner environment.**

**Resting-state fMRI is an offshoot of task-activation fMRI that uses temporal correlations in spontaneous BOLD signal fluctuations between brain regions as a measure of functional connectivity. This (slightly) newer approach to functional imaging is still hobbled by a low SNR but has the distinct clinical advantages of 1) being easy to perform in non-academic imaging centers and 2) allowing for the collection of functional connectivity data in a much broader spectrum of patients. Using this approach, numerous independent groups have identified a consistent set of 15-20 large-scale intrinsic connectivity networks (ICNs) linked to critical sensory, motor, and cognitive brain functions such as vision, hearing, language, working memory, and episodic memory. Scans are typically less than 10 minutes and have been acquired in a host of disease states (advanced dementia, severe depression, and coma for example) that are difficult to study with task-activation fMRI.**

**This talk will examine efforts to develop resting-state fMRI as a clinical marker for various diseases. Biomarkers can be useful for predicting disease in asymptomatic patients, diagnosing disease in symptomatic patients, measuring disease progression, and predicting or confirming response to treatment. Resting-state fMRI studies of several neuropsychiatric disorders including coma, depression, and chronic pain will be considered to illustrate attempts in each of these biomarker domains. The bulk of the talk will focus on attempts to develop resting-state fMRI as a biomarker in Alzheimer's disease and other neurodegenerative disorders. Specific ICNs appear to be targeted by specific neurodegenerative diseases and this relationship can potentially be leveraged to develop sensitive, specific, and dynamic resting-state fMRI biomarkers.**