The rapid imaging renaissance: sparser samples, denser dimensions, and glimmerings of a grand unified tomography

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ABSTRACT

The task of imaging is to gather spatiotemporal information which can be organized into a coherent map. Tomographic imaging in particular involves the use of multiple projections, or other interactions of a probe (light, sound, etc.) with a body, in order to determine cross-sectional information. Though the probes and the corresponding imaging modalities may vary, and though the methodology of particular imaging approaches is in constant ferment, the conceptual underpinnings of tomographic imaging have in many ways remained fixed for many decades. Recent advances in applied mathematics, however, have begun to roil this intellectual landscape. The advent of compressed sensing, anticipated in various algorithms dating back many years but unleashed in full theoretical force in the last decade, has changed the way imagers have begun to think about data acquisition and image reconstruction. The power of incoherent sampling and sparsity-enforcing reconstruction has been demonstrated in various contexts and, when combined with other modern fast imaging techniques, has enabled unprecedented increases in imaging efficiency. Perhaps more importantly, however, such approaches have spurred a shift in perspective, prompting us to focus less on nominal data sufficiency than on information content. Beginning with examples from MRI, then proceeding through selected other modalities such as CT and PET, as well as multimodality combinations, this paper explores the potential of newly evolving acquisition and reconstruction paradigms to change the way we do imaging in the lab and in the clinic.

Keywords: rapid imaging, compressed sensing, sparsity, parallel imaging, MRI, CT, PET, multimodality imaging

"There is in this Earth no maneuver more unnerving than the Spin. Just when one thinks to have advanced into the twilight, Dawn comes round again." – Samuel Bowditch

1. INTRODUCTION

In imaging, we are all spies. Like true intelligence agents or their glamorized counterparts onscreen, imaging scientists and practitioners are charged with gathering critical information in space and time. We employ the latest technology to acquire encoded signals, and deploy laboriously optimized algorithms to decode them. We do what is necessary, piercing the veil of the skin, the skull, the cell, or whatever stands in our way, in order to see what was once invisible.

How did all this undercover work get started? And how is it poised to change in the next few years?

2. BACKGROUND

2.1 A brief history of imaging

The need to resolve both structure and dynamics is a connecting theme across diverse areas of endeavor spanning multiple orders of magnitude in space and time. Examples in the field of biomedical research include visualization of the function and dysfunction of moving organs; characterization of changes in the tumor microenvironment in response to therapy; evaluation of the shifting organization of cellular ensembles during development or disease; tracking of cell membrane permeability changes in response to molecular signals; or exploration of the conformational changes of individual biomolecules upon ligand binding. Increasingly, fields of inquiry ranging from biophysics to genetics to population health all rely upon key technologies for spatiotemporal mapping, display, and interpretation.

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Of course, the development of certain fundamental tools for imaging occurred long before humans arrived on the scene to pursue these kinds of inquiries. The development of a functional eye conferred a notable survival advantage for early organisms such as the trilobite. Note that the trilobite compound eye was already a highly parallel device, capable of extremely rapid imaging. The human eye, with its own parallel photodetector design, evolved together with remarkable reserves of neural processing power. In many ways, the artificial imaging devices devised by humans continue to follow this general model, though they allow us now to see far beyond the limits of our natural senses. The history of biomedical imaging devices, in particular, may be organized according to the characteristic probes used to interact with the body: visible light (augmenting the eye with microscopes, cameras, optical transillumination and tomography devices, etc.), X-rays (ranging from Roentgen's projections in 1896 to X-ray CT in the 1970s), radiotracers (e.g. gamma cameras, SPECT, and PET), electromagnetic fields (e.g. electrical impedance tomography and MRI), mechanical displacements (e.g. ultrasound) – the list goes on.

For the purposes of this report, we shall focus on the tomographic imaging modalities, i.e. the modalities that produce cross-sectional images from sets of acquired projections. When looked at from the right perspective, many of these modalities, such as MRI and CT, are fundamentally alike in their basic principles. Once one has accounted for differences in probe characteristics and scanner engineering, one might be tempted to ask what is new under the sun.

2.2 A brief history of rapid imaging

One facet of imaging that seems always to be on the advance is the speed of image acquisition. In fact, one might argue that there is a natural evolutionary tendency for imaging modalities to get faster over time. This tendency is certainly driven by the inherent inventiveness of those who use imaging devices. It is also driven by a particular selection pressure – namely, the need for speed. In the context of biomedical imaging, this need is obvious and multifold. First of all, patients and organs move, and fast images are required to image moving structures such as the beating heart. Injected contrast agents used to highlight particular internal structures also move, and catching the contrast on its way through the vascular system requires speed. Second, patients get restless. Due to underlying disease or understandable agitation, subjects often cannot sustain long breath-holds, and long total examination times can be challenging. Third, time is money. Scanner throughput, and workflow in general, becomes an important practical consideration in an era like ours of intense cost-consciousness, in which the premium on efficiency is high. Finally, and perhaps most importantly, time is information. Greater imaging efficiency enables the acquisition of more information per unit time, which enhances the value of imaging studies, both for clinical evaluation and for basic research.

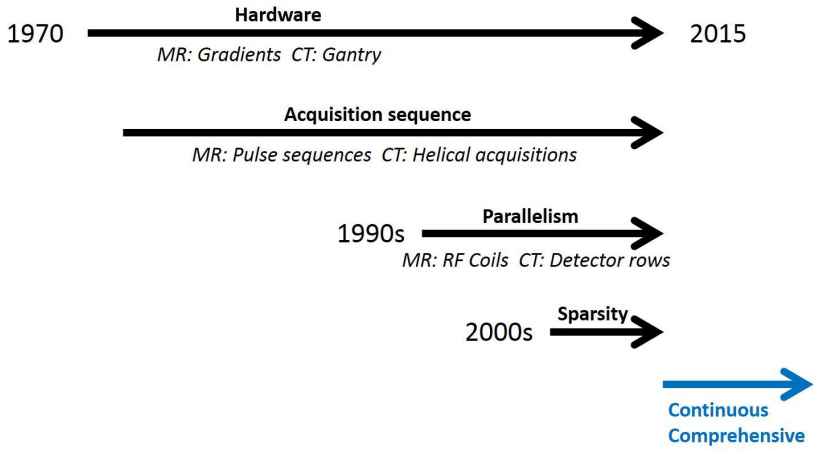


Figure 1. A brief history of rapid MRI and CT.

When viewed through the lens of imaging speed, MRI and CT underwent a strikingly similar evolution since their inception in the 1970s. **Figure 1** summarizes this evolution. Various hardware developments, such as strong and fast-switching magnetic field gradients in MR and rapidly moving gantries in CT, enabled progressively more rapid transitions between sequentially acquired data points. Meanwhile, changes to the acquisition sequence – including rapid MR pulse sequences incorporating rectangular raster patterns (Echo Planar Imaging) or spiral trajectories, and helical acquisitions in CT – further accelerated sequential scanning. It was not until the 1990s that multidetector systems (arrays of RF coils in MR and multiple detector rows in CT) were employed in practice to gather multiple data points

simultaneously, rather than in the traditional sequential fashion. This use of parallelism, which harks back, of course, to the massively parallel configuration of our eyes, enabled further advances in imaging speed beyond previous hardware and software limits. The next decade saw a race to incorporate ever larger numbers of detectors, until this trend, too, began to mature and new practical limits of acceleration began to be reached.

Suddenly, in the middle of the last decade, the landscape of rapid imaging started to shift again. The impetus this time could be traced to developments in the mathematics of image reconstruction. Certainly in the area of MRI, parallel imaging[1-3] had already necessitated substantial changes to image reconstruction algorithms. However, more recent developments had their root in a new appreciation of the role of sparsity and incoherence in the solution of inverse problems like image reconstruction. Modified acquisition approaches were soon being proposed to take advantage of the new reconstruction methods, which tended to be grouped under the label of compressed (or compressive) sensing. Many would argue that we now occupy the era of sparsity in rapid imaging. It is a "post-Nyquist" era, somewhat unsettling to those raised on linear inverse problems, but extraordinarily rich in possibilities for innovation. The outcome in terms of raw acceleration of MR image acquisition is already striking: appropriate combinations of compressed sensing with parallel imaging have, in many cases, been shown to yield order-of-magnitude accelerations as compared with parallel imaging alone. Meanwhile, compressed sensing and related approaches have begun to change the way we view the problem of image formation. Let us now discuss in more detail this disruptive new kid on the block.

3. SPARSITY AND INCOHERENCE: THE RISE OF COMPRESSED SENSING

Compressed sensing may be argued to have arisen out of at least two central observations: 1) that most signals (including images) are simpler than they might at first appear, if they are viewed from the right perspective, and 2) that we can generally control how we encode and decode signals or images, such that undersampling does not necessarily lead to irretrievable loss of information. Over time, numerous particular reconstruction algorithms, taking advantage of various kinds of prior information to reconstruct undersampled datasets, had previously been proposed. However, it is the work of Candès[4], Tao[4], and Donoho[5] that is generally credited with establishing the rigorous theoretical underpinnings of sparse signal recovery from incoherent acquisitions – or, in other words, compressed sensing. Very soon thereafter, Lustig[6] demonstrated concrete applications of compressed sensing for rapid MRI, and in the process created a new subfield of biomedical imaging research.

The fact that we can represent images with less than the usual data is not in itself surprising. It is well known that most images are at least somewhat sparse, in the sense that they may be represented accurately by a number of parameters smaller than the number of voxels. The prevalence of image compression – an essential tool for modern data storage and transmission – serves as concrete evidence of this fact. Image compression algorithms exploit correlations between pixels to reduce the number of bits required for storage. Knowing as we do that most medical images are highly compressible, we are faced with a nagging question: why do we need to exert Herculean effort to acquire fully-sampled data, if in the end we are going to throw most of those data away? Until compressed sensing appeared on the scene, the prevailing answer was that accurate compression requires prior knowledge of image content, so that we can decide which components to discard and which to keep. By definition, however, the content of a new medical image is unknown, and it is in fact the unpredictable abnormalities that represent the most critical information for physicians and their patients. In medical imaging circles, use of prior knowledge is viewed with legitimate caution.

How, then, does compressed sensing effectively accomplish pre-compression without assuming particular image content? It simply asserts that the correct image (or image series) is sparse in a known domain. This domain may be the image domain itself, or it may be defined by transforming the image using Fourier transforms, wavelet transforms, or other operations often used in image compression. Compressed sensing makes no assumption about which coefficients in particular are significant or insignificant – it only assumes that a suitably sparse solution is likely to be correct. Such an assumption does carry risks, but the risks are rather more modest than the risk of corrupting the true image with features of a specific image model.

In practice, successful compressed sensing requires three principal ingredients: 1) sparsity of true image content, 2) incoherent sampling (with incoherence, in this case, assessed between the acquisition basis and the sparse basis), and 3) non-linear reconstruction. The basic principles of compressed sensing are elucidated quite well in the literature, and for particular demonstrations of key concepts as applied to imaging, readers are referred to some of the seminal publications by Lustig et al [6, 7]. A simple and compelling graphical example may be found in Figure 2 of Ref [6] or Figure 5 of Ref [7]. The gist of this example is as follows. The Nyquist theorem dictates that regular undersampling cannot be untangled. When undersampling is performed in an irregular pattern, however, significant components may remain above the

pseudonoise associated with irregular aliasing. Successive thresholding operations, followed by removal of clearly significant components along with their associated irregular aliasing artifacts, can then reveal other previously "buried" components, until the list of significant components is complete.

Mathematically, the compressed sensing image reconstruction problem is often written as follows:

$$\hat{\mathbf{x}} = \arg\min_{\mathbf{x}} \left\{ \left\| \mathbf{E}\mathbf{x} - \mathbf{y} \right\|_2^2 + \lambda \left\| \mathbf{T}\mathbf{x} \right\|_1 \right\} \quad (1)$$

Here, $\mathbf{x}$ represents the true image content, $\hat{\mathbf{x}}$ is the image estimate resulting from reconstruction, $\mathbf{y}$ is the acquired raw data, $\mathbf{E}$ represents the "encoding" operation that converts $\mathbf{x}$ into $\mathbf{y}$ during data acquisition, λ is a regularization parameter, and $\mathbf{T}$ is a sparsifying transform. The first term on the right hand side of Eq. (1) enforces data consistency using a traditional L2 norm, whereas the second term is a sparsity-enforcing regularization term. Note that the use of an L1 norm in the regularization term, substituting for the more computationally challenging L0 norm that would simply count nonvanishing components, enables robust iterative solution using a variety of well-defined numerical methods.

By now, some of the limits of compressed sensing have been well documented. Unlike for many other rapid imaging methods, the maximum acceleration depends upon the underlying degree of sparsity, which may be estimated from experience but which is not known rigorously *a priori*. For a single detector channel, a number of incoherent samples on the order of 3 to 5 times the number of sparse coefficients has been shown to result in statistically reliable information recovery. For multiple detector channels (e.g. when compressed sensing is used together with parallel imaging), the minimum number of samples in each channel approaches the number of sparse coefficients. Meanwhile, there are many practical tradeoffs associated with nonlinear reconstructions of the sort shown in Eq. (1). Simple measures of signal-to-noise ratio (SNR) may no longer be accurate or even sensible, and subtle artifacts may appear when acceleration is excessive or reconstruction is over-regularized. As a result, quantitative image quality evaluation in the presence of compressed sensing may be challenging.

In addition to these potential problematic features, however, there are a number of salutary consequences of adopting a compressed sensing perspective. First of all, one begins to focus less on the number of voxels in an image and more on information content. Second, one is confronted with what might be called a paradox of dimensionality: in the era of sparsity, bigger, more diverse datasets tend to result in better reconstruction performance. Multidimensional datasets tend to demonstrate more sparsity, and enable more incoherence, than datasets with fewer dimensions, and this has led to a new rule of thumb for data acquisition. Whereas in a traditional setting of ordered acquisition and linear reconstruction, simple repeatable sequences are often preferred, in a setting of compressed sensing it behooves one not to repeat oneself. Whenever possible, one should take advantage of temporal coherence and sampling-pattern incoherence. Taken together, these observations connect rapid imaging, more than ever, not just with raw acceleration but also with enhanced information content. The examples that follow, taken largely though not exclusively from experience at our institution, represent only a very cursory sampling of the rich evolving literature in modern rapid imaging.

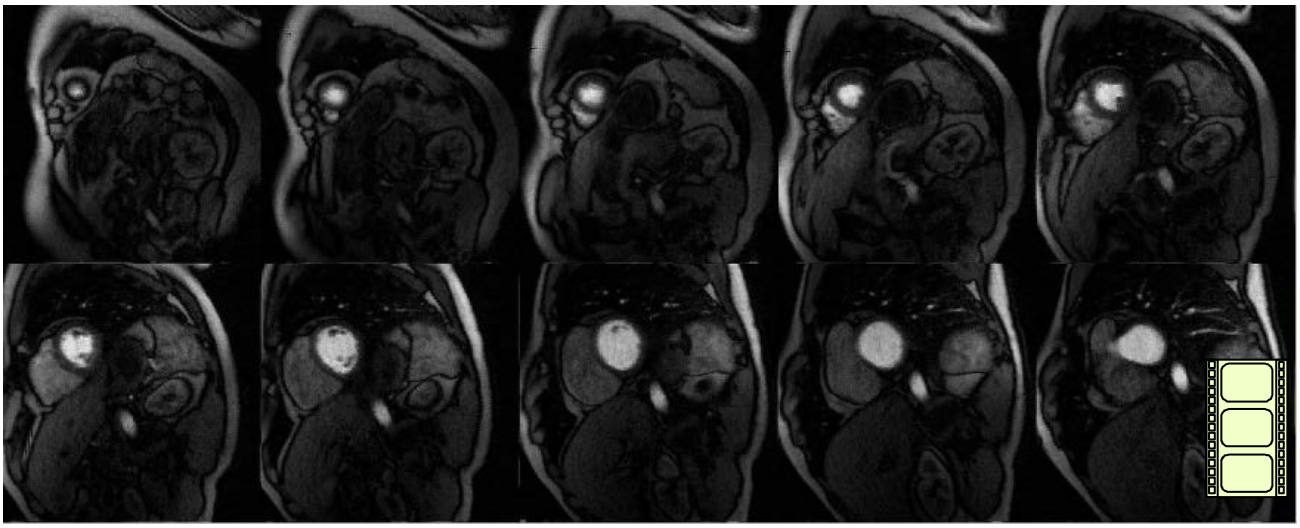
4. THE MANY GUISES OF SPARSITY IN IMAGING

Since the advent of compressed sensing, applications in imaging have burgeoned, particularly in MRI, but increasingly in other modalities. A few illustrative examples are provided here, from MR, CT, and combined MR-PET studies.

4.1 Magnetic Resonance (MR)

Video 1 shows an early example of accelerated multislice first-pass cardiac perfusion MRI[8], taking advantage of a largely synergistic combination of compressed sensing with parallel imaging. In this case, an eight-fold total acceleration enabled whole-heart coverage with 10 slices per heartbeat, temporal resolution of 60ms per slice, and in-plane spatial resolution of 1.7mm. Cardiac imaging, with its competing constraints of spatial and temporal resolution, was one of the earliest areas of implementation for compressed sensing, with numerous reports appearing in the literature and at scientific conferences. Other early clinically-relevant applications of compressed sensing to pediatric MRI were demonstrated by Vasanawala et al[9]. Though scanner vendors have so far been somewhat cautious in introducing compressed sensing into commercial products, research applications by now abound, and various clinical evaluations are underway. One approach that has seen heavy clinical use at our institution is the Golden angle Radial

And Sparse Parallel imaging (GRASP) method[10], which combines continuous radial imaging with compressed sensing and parallel imaging. We shall return to GRASP in the discussion of rapid continuous imaging paradigms to follow.



Video 1. Accelerated cardiac perfusion MRI using a combination of compressed sensing with parallel imaging[8]. The inflow of a gadolinium-based contrast agent is shown in ten short-axis slices acquired in a healthy adult subject. http://dx.doi.org/10.1117/12.2085033.1

4.2 X-ray Computed Tomography (CT)

Radial MR sampling might very well put one in mind of the angular projections acquired using X-ray CT with a rotating gantry. If we were able to undersample CT data in projection space in a fashion analogous to radial MR data undersampling, we would be able to deliver reduced radiation doses to patients (since fewer X-rays would need to be delivered for any given image acquisition). The fact that CT images can be reconstructed from undersampled datasets was recognized at the very start of compressed sensing[4], and proposals for CT dose reduction using compressed sensing appeared soon afterward[11]. However, no practical means of incoherent undersampling, analogous to the methods used routinely in MRI, has yet been demonstrated in the challenging physical environment of a rapidly rotating CT gantry. Our group has recently proposed an undersampling mechanism using a moving multihole collimator[12], and evaluations of this approach for significant radiation dose reductions in CT are underway.

4.3 Positron Emission Tomography (PET) and combined MR-PET

Various uses of compressed sensing may also be envisioned for PET scanning, for applications ranging from spatial resolution enhancement to tracer dose reduction. We will draw our examples here, however, from multimodality image acquisition and reconstruction, enabled, for example, by new simultaneous MR and PET scanners. By and large, multimodality data are currently reconstructed separately, accounting for differences in imaging physics and underlying contrast, and are then superimposed for display. When we acquire simultaneous data on the Siemens mMR MR-PET scanner at our institution, however, these data not only originate from a common anatomy but also share a common acquisition geometry. From a compressed sensing point of view, one might posit that differences between the image content in MR and PET, though substantial, will be sparse in an appropriate domain. Our group has recently proposed a combined reconstruction framework taking advantage of this joint sparsity. Unlike other approaches using MR data as anatomical priors for PET reconstruction, our joint reconstruction approach does not prioritize one modality over the other, and improvements may be seen in both the MR and the PET images, including reductions in undersampling artifacts in MR and improvements in spatial resolution in PET[13]. This form of joint reconstruction may be seen as one example of multi-sensor compressed sensing approaches that are being explored in a range of fields[14-16].

4.4 Hints of a new paradigm

Just as our retinas are enviable models of parallel imaging systems, so we may look to our brains as examplars of sparse information recovery systems. Human neural processes are highly efficient at data compression and information

extraction. As we make our ways through any typical day, our brains are constantly distilling complex inputs rapidly into their essences, and they routinely reconstruct essential information from incomplete input. In considering what is next for biomedical imaging, we might be well served by looking once again to our day-to-day experience of the world. That experience is dynamic and multifaceted, with diverse information streaming in constantly along multiple sensory channels. Can we design imaging strategies to match these aspects of our experience? The next two sections are devoted to early attempts at such strategies.

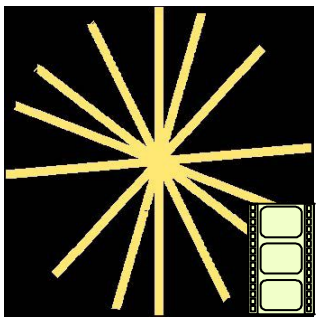
Whereas biomedical imaging protocols have traditionally been designed around well-defined snapshots or ordered series thereof, a paradigm of rapid continuous imaging and flexible image reconstruction is emerging that may be better suited to capture the dynamic nature of experience. Recent continuous acquisition approaches exploit correlations along the time domain, and, in so doing, they may often outperform traditional intermittent acquisition protocols. In keeping with the paradox of dimensionality, it has been shown that acceleration capability, just like compressibility, is much greater with a time series than with a single snapshot, and an incoherently sampled time series plays particularly to the strengths of compressed sensing.

What about the multifaceted nature of experience? We have already spoken of multimodality approaches, such as MR-PET, that can provide simultaneous and complementary information. A more general trend towards rapid comprehensive imaging is now afoot, which aims explicitly to entangle multiple distinct streams of quantitative information, which have traditionally been encoded separately and sequentially, within single dynamic multidimensional datasets. This trend represents a new form of parallelism, which promises to transform imaging devices from "scanners" into something more closely resembling broadband communication channels.

Let us explore some illustrative examples.

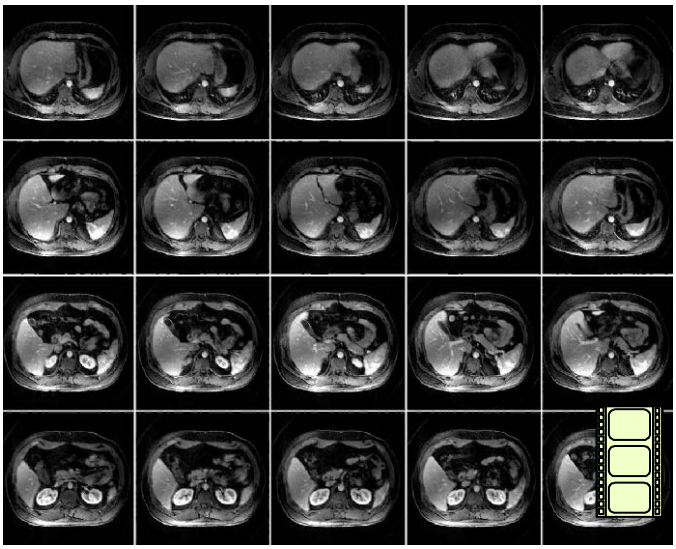
5. RAPID CONTINUOUS IMAGING

Lauterbur's original MR images[17] were obtained with encircling angular projections, which correspond to a radial sampling pattern in Fourier space, or "k-space." Since that time, rectangular "spin-warp" sampling has become the norm. However, there has been a recent resurgence in radial imaging approaches, sparked in large part by considerations of sparsity. Radial k-space patterns tend to have favorably incoherent undersampling properties, well suited to compressed sensing reconstruction. Radial trajectories are also robust to motion, and they lend themselves to flexible angular ordering schemes such as the "golden angle" scheme (see **Video 2**), in which each new radial spoke fills in the largest remaining gap in the angular distribution and provides complementary spatial information in a continuous nonrepeating sequence. The GRASP technique[10] mentioned earlier exploits such a golden angle radial sequence. Since this sequence has no preferred starting or ending point in time or angular distribution, and since even small sets of time-adjacent spokes provide nearly isotropic, if highly undersampled, coverage of k-space, the same dataset may be reconstructed with flexible temporal resolution, at essentially any time point of interest. The limits of achievable temporal resolution in this case depend upon the limits of acceleration that may be attained using parallel imaging and compressed sensing.



Video 2. Animation of a two-dimensional golden-angle radial acquisition sequence, with each new spoke oriented at an angle of 111.25 degrees from the last. This angular pattern can continue indefinitely without repeating.
http://dx.doi.org/10.1117/12.2085033.2

Video3 shows the time evolution of 20 of a total of 40 slices through a series of whole-liver image volumes obtained from a continuous golden-angle radial acquisition following injection of gadopentate dimeglumine[18]. GRASP reconstruction was performed with 1 x 1 x 3 mm^3 spatial resolution and 2.8 second temporal resolution per volume, corresponding to a nominal 20-fold acceleration compared to traditional acquisitions and reconstructions without parallel imaging or compressed sensing. This level of acceleration enables detailed visualization of both contrast agent and respiratory dynamics. Note that one can choose the temporal location of reconstructed time frames retrospectively, so as never to miss the contrast agent bolus. One may also group larger or smaller numbers of spokes into any given time frame, depending upon requirements of spatiotemporal fidelity. Note also that the entire acquisition is performed during free breathing, with no reliance upon the breath-hold capacity of the subject. This flexibility and robustness tends to be greatly appreciated by clinicians. Clinical GRASP studies have been performed for several thousand patients at our institution to date, and GRASP is now being evaluated in multicenter trials. Applications range from head to toe, including abdominal[18], prostate[19], and breast imaging[20] studies, among others.



Video 3. Free-breathing abdominal imaging using GRASP[10, 18]. Twenty slices of a forty-slice whole-liver volume are shown over time during free breathing following the injection of a gadolinium-based contrast agent.
http://dx.doi.org/10.1117/12.2085033.3

Though GRASP is sufficiently motion-robust to obviate the need for breath-holding in many applications, motion can still degrade image quality, either by causing intraframe blurring for low-temporal-resolution reconstructions, or by degrading temporal sparsity and engendering residual inter-frame blurring in high-temporal-resolution reconstructions. Radial trajectories, however, have the additional advantage that each spoke passes through the center of k-space, and this repeated central data may be used as a sensitive indicator of changing motion states. The eXtra-Dimensional GRASP (XD-GRASP) reconstruction method[21] uses inherent self-navigation properties to sort GRASP data into multiple distinct motion states. Rather than simply grouping temporally sequential spokes, the XD-GRASP algorithm groups spokes within a given motion state, and organizes the data into additional temporal dimensions representing the different types of motion. The reconstruction equation then takes the generalized form

$$\hat{\mathbf{x}} = \arg\min_{\mathbf{x}} \left\{ \left\| \mathbf{E}\mathbf{x} - \mathbf{y} \right\|_2^2 + \lambda_1 \left\| \mathbf{T}_1 \mathbf{x} \right\|_1 + \lambda_2 \left\| \mathbf{T}_2 \mathbf{x} \right\|_1 + \ \ldots \right\} , \tag{2}$$

in which a distinct transform $\mathbf{T}_n$ and regularization parameter λ_n may be applied along each dimension. Respiratory motion and contrast enhancement may be captured in distinct dimensions for dynamic contrast-enhanced studies; or, as illustrated in **Videos 4 and 5**, the extra dimensions may represent respiratory motion and cardiac motion for cardiac MRI. (In this case, coils near the heart and the diaphragm are used to characterize the cardiac and the respiratory motion signals, respectively.) Sorting the continuously-acquired data into additional dimensions has a number of advantages. The extra dimensionality results in improved signal sparsity, since disparate motional frequencies and other dynamic characteristics are no longer intermingled. This results in improved image quality and increased acceleration capability. At same time, extradimensional sorting is an efficient means of motion correction, which, unlike some traditional

navigation methods, does not require that any data be discarded. Finally, XD-GRASP enables not just correction for but also characterization of motion. It has been shown to be useful, for example, in separating and visualizing arrhythmic cardiac cycles[22]. It has also proven useful in characterizing respiratory dynamics. **Videos 4 and 5** illustrate some of the scope of new dynamical information to which XD-GRASP provides access. Whereas **Video 4** shows a traditional view of cardiac contraction at a particular phase of respiratory motion, in **Video 5** we sit at a fixed phase of the cardiac cycle and watch the heart over the course of respiration. In this view, we can easily identify septal motion associated with the physiologic phenomenon of left-right ventricular (LV-RV) interaction: a phenomenon which until now has been difficult to visualize directly. Note that all of this information may be obtained from the same continuously acquired dataset, simply by adapting the reconstruction algorithm and by slicing through the resulting multidimensional image series as desired.

Video 4. Results from a cardiac XD-GRASP study[21], showing cardiac motion over time for each of twelve distinct respiratory states identified and sorted using self-navigation data from a continuous free-breathing golden-angle radial acquisition. http://dx.doi.org/10.1117/12.2085033.4

Video 5. More results from a cardiac XD-GRASP study[21], showing respiratory motion over time for each of thirty distinct cardiac phases identified and sorted using self-navigation data from the same continuous free-breathing golden-angle radial acquisition as for Video 4. Note that motion of the interventricular septum during respiration is indicative of the physiologic phenomenon of LV-RV interaction. http://dx.doi.org/10.1117/12.2085033.5

There is still more information to be gleaned from the same datasets. While XD-GRASP enables visualization of distinct motion states, it does not directly quantify the extent of the motion. One could, of course, attempt to coregister distinct frames to derive approximate motion fields. It turns out, however, that one may derive motion fields more directly from within the reconstruction algorithm itself, by appealing to a domain of mathematics closely related to that

of sparse information recovery – namely, low-rank matrix completion. Several years after formalizing compressed sensing, Candès identified a low rank plus sparse (L+S) matrix decomposition of potential value for robust principal component analysis[23]. The separation of correlated low-rank background (L) from sparse innovations (S) has also proven to be valuable for reconstruction of dynamic image series[24]. L+S reconstruction may be viewed as another form of extradimensional reconstruction, in which the S component is rendered sparser by the removal of the background, and in which robust estimation of the background L component may be valuable in itself. Recently, our group has shown that quantitative motion fields may be derived directly from continuously acquired radial data, by self-discovering the frame-to-frame transformations which minimize the rank of the L component[25]. This so-called "motion-guided L+S" reconstruction takes advantage of self-consistency within diverse continuously acquired datasets to derive accurate quantitative motion models, rather than trying to fit the data to a particular *a priori* model.

6. RAPID COMPREHENSIVE IMAGING

The question of quantitation highlights certain notable differences between tomographic imaging modalities. In many ways, quantitative pixel intensities come more naturally to CT and to PET than they do to MRI. The highly flexible tissue contrast and rich endogenous information content associated with MRI also result in a high degree of potential operator- and scanner-dependence. Therefore, whereas the interpretation of most varieties of clinical MR images is qualitative, specialized MR pulse sequences are usually deployed for the quantitative mapping of tissue parameters such as relaxation times or diffusion constants. These specialized sequences come at a significant cost in scan time and, even when carefully calibrated, they suffer from residual errors and interferences which result in undesirable variability.

Recently – and arguably as a partial outcome of the "compressed sensing perspective" alluded to earlier – it has been recognized that the multifactorial complexity of spin dynamics may represent an asset rather than a liability for quantitation. In particular, there is an emerging trend towards fitting multiple physical parameters (and, as desired, deriving multiple contrasts) from the same acquired data. This trend is in direct contradistinction to the traditional approach of designing sequences around as simple a dynamical effect as possible, then correcting for undesired effects though painstaking calibration. Such a trend can also be viewed as another manifestation of the paradox of dimensionality. Whenever possible, the reasoning goes, mix together disparate encoding mechanisms such that the whole dataset is greater than the sum of its parts.

The current archetype of this new comprehensive quantitative mapping approach is the MR Fingerprinting (MRF) technique, as championed by Griswold et al[26]. MRF entangles the effects of multiple physical parameters (T1 and T2 relaxation, proton density, magnetic field inhomogeneity, etc.) in long pulse sequences with irregular timing. Spin evolution under the influence of these sequences results in complex temporal signals that serve as distinctive "fingerprints" for particular sets of parameter values. Individual voxel fingerprints from a series of successive image frames are matched to a database of simulated spin dynamics with a range of known parameter values. Since the MRF sequences are arranged such that undersampling artifacts are incoherent with the dynamical fingerprints, the fingerprints may be matched reliably to the database even for highly undersampled image sets, enabling high degrees of acceleration that compensate for the duration of the lengthy pulse trains. In this way, multiple quantitative parameter maps are derived rapidly and simultaneously from images that, on their own, would be essentially uninterpretable.

Though the simple pattern-matching reconstruction in MRF is quite different from the iterative sparsity-enforcing reconstructions discussed earlier, there is nonetheless a strong connection to compressed sensing. MRF makes liberal use of incoherent acquisition, and Bloch equation models serve to capture the key dynamical coherences in the data, effectively standing in for a sparsifying transform. MRF also has some of the provocative effect of compressed sensing, spurring out-of-the-box thinking about potential new encoding or reconstruction methods. In our group, we have found that, even with more highly coherent acquisitions, for example traditional multi-spin-echo sequences optimized for rapid T2 mapping, one can map multiple quantitative parameters, including not only T2 and proton density but also the B_1^+ RF transmission field distribution, by fitting to Bloch equation models[27]. We have also discovered that MRF pattern matching may be extended to map the B_1^+ transmit field pattern of multiple RF coils[28]. In addition to enriching the information content of fingerprinting sequences at no cost in acquisition time, this new "multi-illumination" fingerprinting approach has been shown to enable robust imaging in the presence of strong RF field inhomogeneities. As a result, it promises to reduce the calibration-heavy and workflow-intensive field of parallel RF transmission to a simple "plug and play" mode of operation[28].

The multiparametric mapping approaches discussed so far all adhere to the general theme of allowing, or even embracing, inhomogeneities and signal imperfections. Rather than employing Herculean efforts to calibrate out imperfections, these approaches quantify inhomogeneities along with the usual desired parameter values, based on the distinctive characteristics of a multifaceted acquired signal. Like XD-GRASP or combined MR-PET, these rapid comprehensive imaging approaches represent a form of all-in-one acquisition. With the example of plug and play parallel transmission, we have also introduced a new theme of workflow simplification, which we will now take up in more depth as our survey of developments in rapid imaging concludes.

7. TOWARD RAPID, CONTINUOUS COMPREHENSIVE IMAGING: THE RAPID IMAGING RENAISSANCE

When it comes to workflow, MRI has much to envy about (and ideally to learn from) CT and PET. Modern multidetector-row CT scanners are capable of comprehensive anatomic coverage in few-second scans. PET scanners gather stochastic 3D radial projections continuously at any given bed position, with minimal user interaction required once appropriate tracers have been injected. By comparison, MR scanning is ponderous and complex, with a profusion of user-definable scan parameters that can, for good and ill, affect the information content of the resulting images. We now offer two examples of how the advances described so far can enable dramatic simplifications of MR (and multimodality) workflow, while preserving and ultimately enhancing image information content.

Cardiac MRI boasts some of the most complex workflow in the field. Both cardiac and respiratory monitoring are routinely performed, and advanced training is required merely to orient key multi-oblique image planes correctly during the planning of scans aimed at characterizing diverse aspects of cardiac anatomy and function. A few-minute comprehensive cardiac examination has long been a holy grail for those interested in cardiac MR. In a collaboration with the research group of Stuber et al., our group is now pursuing a prototype few-minute continuous comprehensive cardiac MR examination, using five-dimensional XD-GRASP[29]. The "spiral phyllotaxis" trajectory[30] used in this work is a generalization to three dimensions of the golden-angle radial trajectory used in prior XD-GRASP studies. In 5D cardiac XD-GRASP, continuously acquired data obtained during free breathing are sorted into cardiac and respiratory motion dimensions, in addition to the three spatial dimensions defining the imaging volume. This approach yields high-resolution isotropic whole-heart image sets in which cardiac motion, respiratory motion, and cardiac anatomy are all resolved. One can obtain robust views of cardiac and great vessel dynamics in any desired orientation, and from the same data one can derive high-resolution depictions of coronary arteries throughout the cardiac and respiratory cycles. In this early work, we have not yet incorporated myocardial perfusion and viability studies, but in light of experience so far using XD-GRASP for other contrast-enhanced studies, this seems a natural extension.

Our second example of rapid continuous comprehensive imaging was also motivated originally by workflow considerations. When we began performing simultaneous MR and PET scans on our Siemens mMR scanner, we quickly realized that the MR imaging protocol in many cases represented a temporal bottleneck. By the time the scan operator was done with gathering the multiple contrast weightings called for in clinical protocols, the typical time needed for FDG-PET acquisitions had long been exceeded. Though of course we could always continue averaging PET counts for the entire duration of the MR protocol, we were in a sense only biding our time. To address this inefficiency, we turned to MRF, and designed a joint MRF-PET acquisition and reconstruction approach[31]. MRF-PET combines joint MR-PET reconstruction, as described earlier, with spin dynamical pattern matching to derive multiple quantitative MR maps together with improved PET images. The joint reconstruction, moreover, improves MR aliasing artifact removal, as a supplement to the incoherence effects in MRF alone. The net result is a diverse, quantitative multimodality image volume obtained in the time normally occupied by a single PET "bed position." **Figure 2** illustrates the range of information which may be obtained from a single six-minute continuous radial MR-PET acquisition. In the figure, only three representative slices are shown out of a total of 30 slices covering the whole head. In addition to the PET image set, matched quantitative T1 and T2 maps are obtained, along with relative proton density maps (not shown). With T1 and T2 values in hand, one can use well-known MR signal equations to generate images with the contrast weightings that would result from any MR pulse sequence of interest, such as the T1-, T2-, and FLAIR weightings shown in the figure. Entanglement of multiple streams of information in this case results not only in improved quantitation but also in marked practical convenience. When all the information of interest may be obtained in a few minutes per bed position, one can begin

to contemplate efficient whole-body MR-PET screening. One can also perform retrospective data mining, in which any suspected lesion detected on MR and/or PET can be examined after the fact with a range of potential synthetic contrasts, to clinch the diagnosis without need for any additional scanning.

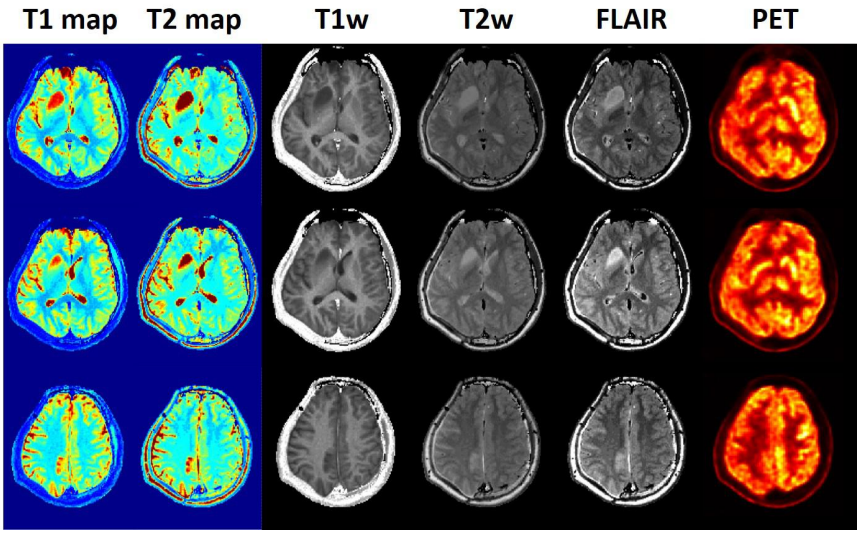


Figure 2. MRF-PET. Three representative slices are shown from a 30-slice whole-brain axial image set obtained after surgery in a patient with a brain tumor. The diverse information obtained from a single continuous six-minute MRF-PET acquisition includes quantitative T1 and T2 maps, jointly reconstructed PET images, and a variety of synthesized contrast weightings, including T1, T2, and FLAIR weightings.

The limits of just how much information can be embedded robustly in sequences like MRF-PET are still being explored. Meanwhile, it is natural to contemplate combining MRF or MRF-PET with approaches like XD-GRASP or motion-guided L+S. Such a combination would address known challenges associated with motion in MRF. It would also represent a unified approach to quantifying physiologic dynamics along with spin dynamics (not to mention PET tracer kinetics). Traditionally, physiologic motion has been considered the nemesis of quantitative imaging, but in such a unified approach, the two would be synergistically entangled, requiring only appropriate reconstruction algorithms to disentangle them as needed.

8. CONCLUSIONS, AND A LOOK TO THE FUTURE

In closing, we would argue that the future of rapid imaging lies in continuous comprehensive data acquisition coupled with flexible image reconstruction. This is why we have included the final arrow shown in blue at the bottom of **Figure 1**. We believe that the rapid continuous comprehensive paradigm has the potential to catalyze a new use of time in imaging, as is illustrated in **Figure 3**. At the top of the figure is a schematic representation of the traditional MR imaging protocol, with distinct contrast weightings achieved in distinct acquisitions using tailored pulse sequences. The scanner is not active during the dead time (D) between each sequence, which may become extended if careful planning of new scan geometries or other user input is required. Motion between scans can hinder registration, and motion during scans typically leads to artifacts. By contrast, the bottom of Figure 3 illustrates the new paradigm of rapid continuous comprehensive imaging. A simple-to-plan comprehensive dataset is acquired efficiently, with no dead time. Patient motion during the acquisition is tracked using self-navigation or motion model discovery. Depending upon the clinical indication for imaging, a preset portfolio of reconstructed images may be presented initially to the radiologist. If he or she detects anything in these images which raises suspicion, and which calls for any new views or contrasts, these may be generated on the spot from the raw data by appropriate reconstruction or other processing algorithms. The acquired data, moreover, need not be limited to MR data. If multiple modalities are available, then joint reconstruction may be applied to take advantage of shared information, to highlight noteworthy differences, and, ultimately, to generate multimodality "fingerprints" of pathology.

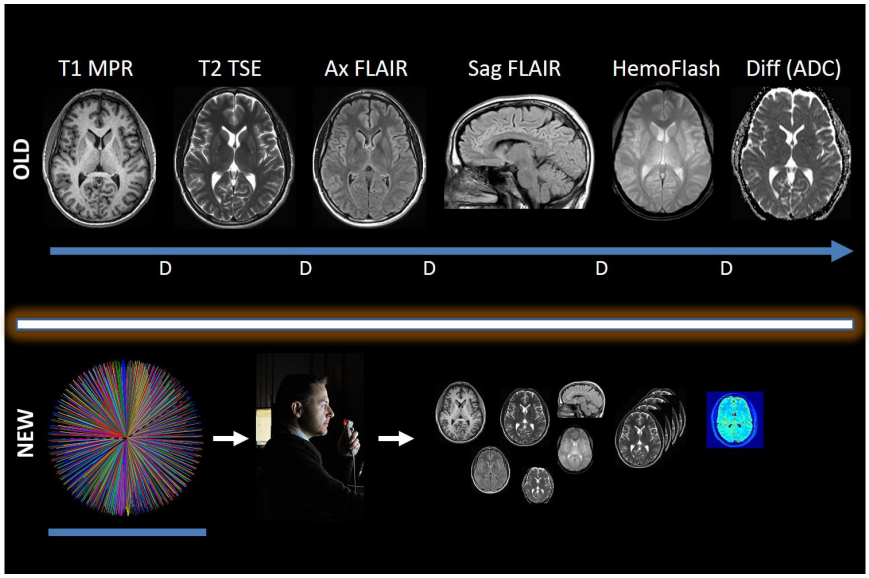


Figure 3. Towards a new use of time in imaging. Top: schematic illustration of a traditional ("old") MR imaging protocol. (D = dead time between distinct contrast-weighted sequences.) Bottom: illustration of the new paradigm of rapid continuous comprehensive imaging.

Despite the technological and computational complexity underlying such a continuous comprehensive imaging paradigm, its net effect will be a marked operational simplicity. One can envision a future scanner operator's tasks being distilled down to a) positioning the subject within the scanner, and b) pressing the "go" button. The key challenge then will lie in navigating the resulting multifaceted datasets. This is a worthy challenge, which is already being taken up across a broad range of disciplines in our increasingly information-saturated age. In the meantime, much work remains to be done before the current rapid imaging renaissance reaches its peak. We encourage students of imaging to embrace the disruption and the opportunity that will ensue. The result may be nothing less than a change in the way we see the world around us.

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