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Invited article

An equation-free introduction to post-mortem MR image contrast and pulse sequence optimization

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ABSTRACT

Due to the excellent sensitivity of Magnetic Resonance (MR) imaging to subtle differences in soft tissues, MR enables non-invasive anatomical imaging with superior soft tissue contrast relative to X-ray Computed Tomography (CT). However, relative to the X-ray modalities, the utility of MR in the post-mortem setting is currently less well-defined. MR is significantly different from the X-ray modalities, in terms of the underlying principles of image formation, the equipment and expertise necessary to acquire the images, and the appearance of the images themselves. Because MR is sensitive to subtle differences in soft tissues, factors unique to the post-mortem setting, particularly variations in body temperature, tend to have a greater effect on MR imaging relative to the X-ray modalities. Fortunately, MR is inherently flexible and adaptable; there are many types of MR protocols, each with user-controlled parameters that can be adjusted to achieve the best imaging of a specific pathology or anatomic structure, at a given temperature or post-mortem interval (PMI). Optimizing, validating, and standardizing post-mortem MR (PMMR) protocols represents a challenging yet achievable long-term goal. For those interested in developing a better understanding of how to optimize PMMR image quality, this review is intended to provide some guidance, from a technical (but non-mathematical) perspective. A practical explanation of basic pulse sequences and MR relaxation times, and their relationship to tissue contrast, is provided. Strategies for optimizing PMMR for forensic imaging applications, suitable for users with varying levels of expertise, are discussed in the context of current progress in this area.

1. Introduction

Radiography was invented in 1895 and was enthusiastically applied the same year to both clinical subjects and forensic investigation [1]. In contrast to Radiography, three-dimensional (3D) non-invasive imaging techniques–including X-ray Computed Tomography (CT) and Magnetic Resonance (MR) imaging–require computation in order to transform the acquired data into an image. Thus, the introduction to clinical medicine of CT in the 1970's and MRI in the1980's naturally followed the commercial availability of "mini-computers" [2], which began around 1960. Additionally, the early development of nuclear magnetic resonance (NMR) techniques in the 1950's benefited from advances in radiofrequency signal generation and detection made by scientists working on radar during the 1940's [3].

Today, CT and MR are workhorses in clinical medicine, and they are finding increasing application in the forensic imaging setting [4]. Following the introduction of MR to clinical practice in the 1980's, the first reports of forensic applications were published ca. 1990 [e.g., [5–7]]. Early studies of the utility of PMMR (post-mortem MR), relative to autopsy [e.g., [8–10]] were undertaken during the 1990s, resulting in expressions of both optimism [11] and pessimism [12] regarding the future of PMMR and forensic imaging in general. Since that time, the field has matured considerably. The current status of PMMR evaluation of adult subjects was recently reviewed by Ruder et al., who describe a number of forensic applications for which PMMR is currently proving useful, including whole body coronal surveys using T2-weighted imaging to screen for pathological fluid accumulations and the use of PMMR for visualizing a number of pathologies of the heart, brain, subcutaneous fat, and abdominal organs [13]. These authors also provide recommendations regarding which clinical MR protocols perform most reliably in the PM setting, while at the same time noting that the current lack of optimized, general-purpose PMMR protocols is a limitation for some applications. Arguably, post-mortem imaging of infants and fetuses is the most well-studied PMMR application to date [14–16]. A recent prospective study assessed the accuracy of whole body PMMR using the MaRIAS

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(Magnetic Resonance Imaging Autopsy Study) protocol [17] in comparison to conventional autopsy in a cohort of 400 fetuses and children (< 16 y) [14]. Overall, the study demonstrated that the cause of death or other major pathologies found by PMMR had an 89% concordance with the findings of conventional autopsy, with the highest concordance observed in the fetal subgroups (94.6% and 95.7% for < 24 weeks and > 24 weeks gestation, respectively). Studies of this type mark a milestone in the maturation of the PMMR field, and they are critical for providing the evidence basis to justify increased use of (and continued research investment in) PMMR in forensic practice.

In the meantime, MR imaging technology continues to evolve. Primarily driven by clinical medicine, ongoing improvements in scanner technology are improving the sensitivity and spatial resolution of MR, and new types of acquisition sequences are under development to increase imaging speeds or take advantage of newly-identified contrast mechanisms. Therefore, questions about the utility of PMMR in the forensic setting must be revisited on a regular basis, taking into account the latest advances in both the clinical and forensic realms. Continuing efforts to optimize PMMR protocols will necessarily be an iterative and cooperative process, as the technology continues to improve, as forensic practitioners gain increasing familiarity with PMMR, and as clinically-trained MR specialists (technologists, radiologists, and physicists) hone their expertise in adapting MR to the post-mortem setting.

This review is intended to provide some guidance, from a technical (but non-mathematical) perspective, to anyone interested in developing a better understanding of how to optimize PMMR image quality. A practical explanation of basic pulse sequences and MR relaxation times, and their relationship to tissue contrast, is provided. Strategies for optimizing PMMR for forensic imaging applications, suitable for users with varying levels of expertise, are discussed in the context of current progress in this area.

2. MR imaging fundamentals

2.1. X-ray imaging: an old friend

To ease into the topic of how MR works, it is helpful to first think some about X-ray imaging. In Radiography, an image of a subject's anatomy is formed by exposing one side of a subject to an X-ray beam, and then detecting the X-rays that pass through the subject on a two-dimensional (2D) image receptor on the opposite side. Prior to the availability of computers, photosensitive film was used (very successfully) to capture, view, and store the images. For X-ray computed tomography (CT), which enables 3D imaging, the basic physical principle is the same, but the geometry is different. CT utilizes collimated sources and small detectors, mounted on opposite sides of a ring, enabling image data to be gathered along a helical trajectory that winds around the subject. Transforming the raw helical data into an image would be very time-consuming without a computer. The source of image contrast in Radiography and CT is relatively easy to understand – lower density tissues, such as muscle, allow more X-rays to pass through, compared to higher density tissues, such as bone; thus the grayscale values are related to tissue densities. Conventionally, light and dark have the same basic meaning in Radiographic and CT images – in general, bones appear white, soft tissues are an intermediate shade of gray, and air appears black.

2.2. MR basics: how is MRI different?

Like CT, Magnetic Resonance (MR) imaging involves collecting raw data (which looks nothing like the subject) and using a computer algorithm to transform the data into an image. However, the physical principles of MR signal generation and spatial localization are completely different from those of the X-ray modalities, resulting in a different imaging appearance and unique advantages and limitations. While X-ray and CT are somewhat analogous to photography, MRI is actually more analogous to radio.

To begin thinking about MR imaging, consider that mammals are mostly made of water, which is dense with hydrogen atoms, and hydrogen nuclei are weakly magnetic. While the magnetism of one hydrogen nucleus is too small to be easily detected, by exposing a drop of water to a strong magnetic field, the magnetism of all of the hydrogen nuclei together is large enough to produce a detectable signal [18]. To create and detect this signal, a clinical MR scanner utilizes a strong magnet, a radiofrequency coil, and some electronics. Once the hydrogen atoms in a subject have been magnetized by the strong field from the magnet, the coil and electronics function like a two-way (transmit/receive) radio set. In MRI, all of the hydrogen nuclear magnets in some volume of the subject can be made to rotate cooperatively by transmitting radio waves of the correct frequency into that volume. The cooperative rotation ("Magnetic Resonance") creates a detectable voltage in the coil, which is placed around (or near) the volume of interest. The rotation of the hydrogen nuclear magnets occurs at a frequency of 63 MHz (in a 1.5 T field) or 126 Mz (at 3 T), a frequency range that overlaps that of television and FM radio transmissions.

2.3. MR pulse sequences: what is pulsing…and why is it so LOUD?

MR acquisition protocols involve transmitting strong bursts of radio waves ("pulses") and then detecting the much weaker signal (the "echo") from the subject. Electric circuits mounted inside the main magnet (the "gradients") generate additional magnetic fields whose intensities vary with position. The gradients are also pulsed on and off to encode the received MR signal with information about the location of the hydrogen nuclei, enabling the transformation of the received signals into an image. MR acquisition requires repeating this "pulse sequence" multiple times to build up a data set with sufficient signal intensity and spatial information [19].

An MR pulse sequence is typically characterized by an echo time (TE) and a repetition time (TR), as shown in Fig. 1. TE is generally the time between the first radiofrequency pulse in the sequence[1] (the "excitation pulse") and the detected signal (the "echo"). TR is the time between successive excitation pulses. Unfortunately, the pulsing process is loud, because rapidly switching the gradient pulses on and off creates mechanical vibrations with frequencies roughly in the middle of the range of human hearing. TE is typically tens of milliseconds, and the sequence of chirps and buzzes repeats with an overall rhythm set by TR, which is typically hundreds of milliseconds up to several seconds.

2.4. MR relaxation: sometimes change is a good thing

If MR detects hydrogen, then one might ask, "Doesn't the tissue contrast simply depend on hydrogen density?" Indeed, if hydrogen density were the only factor controlling the signal intensities, then the soft tissue contrast in MR would be somewhat similar to that of CT, and perhaps there would be not be a good reason to do MR. However, the soft tissue contrast is generally superior to that of CT,

[1] Some pulse sequences use additional pulses to "prepare" the magnetization in a particular state prior to excitation, in which case the excitation pulse is not actually the first pulse in the sequence. Inversion-recovery preparation (used in FLAIR and STIR sequences, for example) employs an extra preparatory pulse to rotate the magnetization 180°. The delay between the inversion pulse and the excitation pulse is the inversion time (TI).