Magnetic resonance imaging and computed tomography of the brain - 50 years of innovation, with a focus on the future

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Abstract: This review focuses specifically on the developments in brain imaging, as opposed to the spine, and specifically conventional, clinical, cross-sectional imaging, looking primarily at advances in magnetic resonance imaging (MRI) and computed tomography (CT). These fields are viewed from a perspective of landmark publications in the last 50 years and subsequently more in depth using sentinel publications from the last 5 years. It is also written from a personal perspective, with the authors having witnessed the evolution of both fields from their initial clinical introduction to their current state. Both CT and MRI have made tremendous advances during this time, regarding not only sensitivity and spatial resolution, but also in terms of the speed of image acquisition. Advances in CT in recent years have focused in part on reduced radiation dose, an important topic for the years to come. Magnetic resonance imaging has seen the development of a plethora of scan techniques, with marked superiority to CT in terms of tissue contrast due to the many parameters that can be assessed, and their intrinsic sensitivity. Future advances in MRI for clinical practice will likely focus both on new acquisition techniques that offer advances in speed and resolution, for example, simultaneous multislice imaging and data sparsity, and on standardization and further automation of image acquisition and analysis. Functional imaging techniques including specifically perfusion and functional magnetic resonance imaging will be further integrated into the workflow to provide pathophysiologic information that influence differential diagnosis, assist treatment decision and planning, and identify and follow treatment-related changes.

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Magnetic Resonance Imaging and Computed Tomography of the Brain—50 Years of Innovation, With a Focus on the Future

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Abstract: This review focuses specifically on the developments in brain imaging, as opposed to the spine, and specifically conventional, clinical, cross-sectional imaging, looking primarily at advances in magnetic resonance imaging (MRI) and computed tomography (CT). These fields are viewed from a perspective of landmark publications in the last 50 years and subsequently more in depth using sentinel publications from the last 5 years. It is also written from a personal perspective, with the authors having witnessed the evolution of both fields from their initial clinical introduction to their current state. Both CT and MRI have made tremendous advances during this time, regarding not only sensitivity and spatial resolution, but also in terms of the speed of image acquisition. Advances in CT in recent years have focused in part on reduced radiation dose, an important topic for the years to come. Magnetic resonance imaging has seen the development of a plethora of scan techniques, with marked superiority to CT in terms of tissue contrast due to the many parameters that can be assessed, and their intrinsic sensitivity. Future advances in MRI for clinical practice will likely focus both on new acquisition techniques that offer advances in speed and resolution, for example, simultaneous multislice imaging and data sparsity, and on standardization and further automation of image acquisition and analysis. Functional imaging techniques including specifically perfusion and functional magnetic resonance imaging will be further integrated into the workflow to provide pathophysiologic information that influence differential diagnosis, assist treatment decision and planning, and identify and follow treatment-related changes.

Key Words: brain, magnetic resonance imaging, central nervous system, computed tomography, gadolinium, technology

Studies published in Investigative Radiology that have received the highest number of citations (specifically the top 250) include a diverse but critical set of advances for our field. In this section, 10 important central nervous system (CNS) studies are highlighted. The number 4 most cited study quantitates the relaxation properties of the commercially available gadolinium chelates at the clinically relevant field strengths used today, 1.5 and 3 T.† This article also serves as the reference standard in the field, although it is likely to be displaced with time by a more recent publication in the journal, which expands the comparison to include 1.5, 3, and 7 T, and specifically compares the agents in the most relevant environment, that of human blood.‡ One focus of the journal historically has been contrast media, and the appearance of an additional study in the top 50 is not surprising. The number 21 on this list is the first demonstration of significant differences in relaxivity between extracellular gadolinium chelates, depending upon their design. This is a potentially important differentiator between agents, with implications in routine clinical use.¶ The 31st most cited study introduces the topic of mean transit time in computed tomography (CT), launching the field of cerebral perfusion for cross-sectional imaging,§ which is now a widely used clinical measure for both CT and magnetic resonance imaging (MRI). Evaluation of cerebral ischemia and neoplastic disease today incorporates measurement of cerebral blood volume, in the first disease category for prognosis and therapeutic decision making and in the second for differential diagnosis. Also in the top 250 cited articles is the first description of diffusion-weighted imaging (DWI),∥ and its potential as an important additional noninvasive MR marker. The importance of diffusion imaging lies only just behind the fundamental parameters of T1 and T2, and once available was rapidly integrated into clinical routine. Additional critical advances in CT that are highlighted by articles in the top 250 cited studies include the first description of sagittal and coronal reformatted images obtained from axial scanning¶ and the first description of stereotactic head frame use.‡ Both techniques are now routinely used and today represent standard clinical practice. In MRI, additional important advances highlighted by articles include the first demonstration of brain mapping (functional magnetic resonance imaging), which was shown for the visual cortex,∥ the advent, challenges, and advantages of 3 T for brain imaging,¶ and the description of an early important contraindication for MR, the presence of a deep brain stimulator.† Another landmark article in the top 250 articles published concerns health policy, specifically the evaluation of research methods/publication by disease, level of impact, and quality of research.∥

The past 5 years of publications in Investigative Radiology were evaluated in greater detail, looking for trends as well as important focus areas. Forty references from this period are highlighted, and they establish the most important areas of CNS research for the next decade, as well as the disease entities of greatest focus (cerebral ischemia and CNS neoplasm). Regarding cerebral ischemia, the focus in the radiologic literature is predominantly on improved imaging technique. Computed tomography has developed to the extent that whole-brain perfusion is now possible, being previously limited to only a few slices.¶ This of itself is a critical advance but just as important is the acquisition of such data with markedly lower radiation dose (Fig. 1). Widespread availability of CT perfusion today makes triage of patients presenting with clinical symptoms of ischemia possible, which is of critical importance relative to therapy. The availability of CT perfusion also has had other benefits, for example, improving detection of smaller ischemic lesions.∥ Automated CT techniques, based on image processing alone or on the characterization of tissue using dual-energy CT, will eventually be a part of mainstream clinical practice, improving lesion detection and characterization. Automatic detection and volume estimation of infarcts, in particular acute infarcts that are quite subtle on CT, is well within the grasp today of computer technology.¶ In another example, the limited ability to differentiate between hemorrhage and calcification within lesions still detracts from the clinical value of CT, with dual energy offering a major advance in this role.∥ Color-coded CT angiography, a new method of displaying dynamic cerebral CT angiography, provides the individual interpreting the exam with important additional diagnostic

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Further developments in MRI technique, both acquisition and postprocessing, should have major impact upon utilization of this modality over the next decade. Innovative studies in Investigative Radiology illustrate the current advances being made in MR angiography (MRA), quantification of perfusion and permeability, detection and quantification of iron, further image acquisition techniques for improved lesion detectability and quantification, and new functional evaluations, with mainstream application for large clinical subpopulations. The likely focus of MR development in the next decade will be in image reconstruction and postprocessing, rather than new acquisition sequences with different tissue contrast, and specifically involving the field of data sparsity. For conventional imaging, this approach has the potential for a 2-fold to 4-fold increase in scan speed, whereas in dynamic techniques such as MR angiography, the potential is on the order of more than 10-fold.

The field of 7 T is very much in its infancy in terms of routine clinical use in the brain. Future clinical scanners might not be 7 T per se but simply substantially higher in field strength than the premier clinical 3 T MR systems of today. It is also possible that such ultrahigh field scanners might develop a niche for clinical imaging in the high-end private world (with direct fee for service), which has the financial resources to purchase and maintain such systems, and which is also not dependent upon medical insurance plans and reimbursement. Advances are ongoing in brain imaging, with clinical studies based on scanner and sequence acquisition advances demonstrating the potential for brain imaging at an intrinsic resolution and with tissue contrasts not possible at 3 T (Fig. 3). As with other specific techniques such as susceptibility-weighted imaging, time of flight magnetic resonance angiography at ultrahigh field should be markedly superior to that at 3 T. Advances in TOF imaging technique are ongoing, with amelioration of SAR constraints enabling venous suppression, improving excitation fidelity, leading to higher contrast, and achieving smooth slab transitions. Carotid imaging at 7 T has attracted substantial attention, given the importance of spatial resolution in evaluating the carotid wall and atherosclerotic disease. Other specialty areas within the CNS where ultrahigh field MR could easily surpass 3 T in terms of diagnostic efficacy include the orbit, sella, and internal auditory canal. These are all areas where signal-to-noise ratio (SNR), contrast-to-noise ratio, and spatial resolution are critical for diagnosis. Although imaging of other nuclei has yet to have a clinical impact (despite early predictions, which were made even for imaging at 1.5 T), ultrahigh field MR offers greater potential in this area. Early imaging results for sodium in the evaluation of astrocytomas reveal its value for differentiation on the basis of tumor grade, as well as providing additional lesion characterization.

Magnetic resonance–positron emission tomography (PET) resembles in its development the field of MR itself. Its introduction was...
marked by very high costs and long exam times, with acceptance limited as well by the existence of a prior well-validated competitor, PET-CT (the competitor for MR upon its introduction was CT itself). MR-PET offers many advantages, such as true simultaneity of acquisition, the possibility of diffusion tensor imaging, and metabolic mapping with spectroscopy. Validation studies with the first commercial units show excellent quantification and stability, with more than 50 units in place worldwide as of 2015.

Substantial advances have also occurred in CT brain imaging in the last 5 years, with the latest scanner and software design providing multiple mechanisms to lower radiation dose. Of importance for brain is the use of lower kV (≤80), offering both lower radiation dose and higher sensitivity to iodinated contrast media. This is particularly important for CT angiography.

Not to be overlooked in this assessment, however, is the marked improvement in image quality and imaging technology over the past decades (Fig. 4). This is for all modalities, including MR, CT, and digital subtraction angiography. For example, the latter (flat panel CT) can now provide excellent cross-sectional images, with soft tissue contrast approaching that of dedicated CT units. Overall image quality has advanced to a remarkable extent, in particular for MR, with scan times decreasing by factors of 10 to 100 since the early 1980s. In regard to intravenous contrast media for CT (and digital subtraction angiography), the nonionic iodinated contrast media have now replaced their

![FIGURE 4](image4.png)

**FIGURE 4.** State of the art in 1984, a patient with multiple sclerosis (A). The images were acquired at 0.5 T, with a voxel size of 10 × 2.2 × 2.2 mm³. Both images were acquired using 3D spin echo technique, with scan times respectively of 47 and 37 minutes. The left-hand image is T1-weighted, an inversion recovery technique, and the right-hand image is T2-weighted, however, with repetition time = 1000 milliseconds. This is compared to state-of-the-art images in 2015 (B), also in a patient with multiple sclerosis, imaged at 3 T. DIR indicates double inversion recovery EPI acquisition (readout segmentation of long echo-trains) or on the order of 5 minutes or less for each imaging sequence. Reprinted with permission from Runge et al (AJNR Am J Neuroradiol. 1984;14:1015–1026) and Runge et al (Neuroradiology: The Essentials with MR and CT. New York, NY: Thieme Medical Publishers; 2015).

In addition, 1988 marked the clinical launch of the gadolinium chelates for MR as intravenous contrast media. In the latter field, there has been a recent trend toward use only of the macrocyclic agents because of their superior safety profile. The gadolinium chelates are critical to diagnostic MRI of the CNS, with more than 300 million total administrations to date worldwide, and approximately 30 million

![FIGURE 5](image5.png)

**FIGURE 5.** The efficacy of a gadolinium chelate for improving lesion detection and differential diagnosis in the brain was first shown in 1984, using a dog brain abscess model. This work received the Dyke award that year from the American Society of Neuroradiology. A coronal postcontrast T1-weighted image at 0.5 T is presented from that research (A), together with the matching enhanced coronal CT, both depicting a large ring-enhancing lesion. Today, intravenous contrast administration is broadly applied for brain imaging in MR with widespread utility. Images obtained at 3 T in a patient with metastatic melanoma are presented, both precontrast and postcontrast. Although several small lesions are visualized in the frontal lobes, precontrast (likely due to hemorrhage), the devastating extent of disease in this patient is only evident postcontrast. Reprinted with permission from Runge et al (AJNR Am J Neuroradiol. 1985;6:139–147) and Runge et al (Neuroradiology: The Essentials with MR and CT. New York, NY: Thieme Medical Publishers; 2015).

![FIGURE 6](image6.png)

**FIGURE 6.** MRI at 3 T of a small cortical acute infarct (arrow) illustrating simultaneous multislice accelerated diffusion-weighted echo planar imaging. The advent of this technique is analogous to that of multislice 2-dimensional imaging in the 1980s, and as such may represent one of the major image acquisition innovations in the current decade with widespread clinical applicability. Using an acceleration factor of 3 in combination with a reduction in slice thickness, 2-mm sections through the entire brain can be acquired in a reasonable scan time, with image quality (and SNR) comparable to the 4-mm standard diffusion-weighted EPI acquisition. Because of the thicker section (4 mm), this small cortical infarct was not seen on the conventional readout segmented DWI acquisition (readout segmentation of long echo-trains) or on the accelerated 2-band scan but was noted on one of the two 2-mm sections acquired at this level, an advance made possible by the use of slice acceleration and in this instance 3 bands.

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enhanced MR procedures per year. Half of these are for CNS imaging, where the gadolinium chelates play a critical role for both disease detection and differential diagnosis (Fig. 5). Evaluation of tissue perfusion, and contrast-enhanced MRA, would also not be possible without this class of contrast media. Research into development of a new generation of contrast media is ongoing for both CT and MR, with the reader referred to the specific article in this issue of Investigative Radiology focusing on intravenous contrast media.

Two software developments in MRI, slice acceleration and sparse sampling, which will see continued attention over the next decade, deserve discussion because of their potential impact long term. For slice acceleration techniques (simultaneous multislice or multiband imaging), the work to date is most advanced involving echo planar imaging, with suggestion of standardization using a tilt in the axial plane. In the example presented (A), improved depiction of enhancing tumor (arrow) is noted in the left lobe frontal lobe with this approach. Standardization of imaging plane is an important key today to good clinical practice (B), with automatic image alignment (if implemented by the technologist) as a standard part of prescan adjustments. Watershed infarcts are presented on FLAIR images from an examination the week after clinical presentation (left column) and at 3 months (right column). Images in the upper row are the original axial reformatted images from the 3D data sets; the images in the lower row are reformatted to match imaging plane for the 2 examinations. Note that by standardization of the displayed imaging plane, the larger deep white matter infarct on the right (white arrow) can now be easily identified on the follow-up examination, and its evolution assessed, with gliosis replacing the previously identified edema, in a slightly smaller area of involvement, with central cavitation. Comparison of a cortical lesion in the superior parietal gyrus on the left (black arrow), now enabled by the standardization of the presented axial plane, reveals extensive resolution of edema with only a pinpoint area of gliosis remaining. Reprinted with permission from Runge et al (Magn Reson Imaging. 1987;5:421-430) and Runge (Imaging of Cerebrovascular Disease. New York, NY: Thieme Medical Publishers [in preparation]).

There is also a need in the future to look critically at the implementation in clinical imaging of the available sequences, both to assure the choice of imaging technique that is most sensitive and to standardize quality and time efficiency for maximum throughput (Fig. 7). The latter is a continuing mandate by the medical insurance system and the governments of the G7. An example of the former is the need for better dissemination of knowledge concerning the most sensitive scans techniques for disease detection, with a primary example being screening and follow-up examinations for intracranial metastatic disease.

One important remaining topic is that of diffusion tensor imaging (and next-generation diffusion MR), with future development benefiting from many of the innovations and advances previously described. The signal in DWIs is mainly determined by the microstructure of a cell and its organelles (on the scale of micrometers), in distinction to that of T1- and T2-weighted images, which is mainly determined by molecular structures (on the scale of nanometers). Precise analyses of diffusion MR provide intracellular and extracellular fraction changes of water (conventional DWI), axonal/myelin-sheath direction and deterioration (diffusion tensor imaging), and other microstructural information such as axonal diameter (Q-space imaging and other next-generation diffusion metrics). Diffusion MRI is used in quantitative analyses, as well as structural connectivity analyses of the brain (Fig. 8) and the spinal cord.

FIGURE 7. Then and now, standardization of image tilt. As early as 1987, inconsistent head positioning was recognized as a problem in clinical imaging, with suggestion of standardization using a tilt in the axial plane. In the example presented (A), improved depiction of enhancing tumor (arrow) is noted in the left lobe frontal lobe with this approach. Standardization of imaging plane is an important key today to good clinical practice (B), with automatic image alignment (if implemented by the technologist) as a standard part of prescan adjustments. Watershed infarcts are presented on FLAIR images from an examination the week after clinical presentation (left column) and at 3 months (right column). Images in the upper row are the original axial reformatted images from the 3D data sets; the images in the lower row are reformatted to match imaging plane for the 2 examinations. Note that by standardization of the displayed imaging plane, the larger deep white matter infarct on the right (white arrow) can now be easily identified on the follow-up examination, and its evolution assessed, with gliosis replacing the previously identified edema, in a slightly smaller area of involvement, with central cavitation. Comparison of a cortical lesion in the superior parietal gyrus on the left (black arrow), now enabled by the standardization of the presented axial plane, reveals extensive resolution of edema with only a pinpoint area of gliosis remaining. Reprinted with permission from Runge et al (Magn Reson Imaging. 1987;5:421-430) and Runge (Imaging of Cerebrovascular Disease. New York, NY: Thieme Medical Publishers [in preparation]).
In summary, advances in technology have speeded the evolution of both CT and MR as clinical modalities, a process made possible in part by the concurrent evolution of computers, enabling control of the scanners, data handling, and image reconstruction as we know it today. Much of the innovation was driven by the growing importance in clinical medicine of cross-sectional imaging for disease diagnosis and treatment evaluation. Imaging of the brain today occupies a central role in medical care in regard to any question of CNS involvement or symptoms. This represents a marked change and critical advance from 50 years ago (1965) when diagnosis relied upon plain radiographs, pneumoencephalography, and cerebral (x-ray based) angiography.

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