Neuroradiology - Where Quantitative Imaging Helps Making a Better Diagnosis

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Lesion Perfusion

- There is mild hypodensity involving the right lentiform nucleus together with a hyperdense right MCA sign.
- A large hyperacute right MCA distribution infarct is confirmed on CBV and TTP maps, from the perfusion CT study.
- There is a mismatch between the smaller core of infarcted tissue seen on the CBV study and the larger penumbra, or tissue at risk, as identified on the TTP map, suggesting that the lesion may be amenable in the acute setting to therapy.
- Clinical presentation was within a few hours of symptom onset, with CT, MR and DSA performed in a rapid temporal sequence.
- The area of ischemia is well identified on the TTP image, with a smaller area of abnormal CBV.
On MR, only a small area of abnormality involving the white matter of the corona radiata is noted on DWI.

There is a paucity of left MCA branches on TOF MRA, reflecting occlusion or slow flow.

MTT and CBV derived from the MR study demonstrate similar findings to CT, with a large diffusion perfusion mismatch ("penumbra" or tissue at risk).
• DSA performed prior to and following thrombectomy demonstrates recanalization of the superior MCA trunk.
Other Quantitative Applications

- Restricted diffusion within the lesion correlates clinically with higher tumor grade and poorer prognosis.
- CBV and CBF also correlate well with histopathologic grade, and can be used to differentiate a low-grade glioma from an anaplastic astrocytoma and from a glioblastoma, being highest in the latter.
- On MR spectroscopy there is decreased NAA (a marker of neuronal integrity) and increased choline (a marker of increased cellular turnover), consistent with neoplastic disease.
Other Quantitative Applications

- CBV is decreased in radiation necrosis (and elevated in recurrent tumor)

- Meningiomas, glioblastomas, and metastases have high CBV, with CBV low in lymphoma
Preoperative assessment of the corticospinal tract can be accomplished in patients on MR by integrating fMRI data with diffusion tensor tractography. In this patient with a cavernous malformation in the precentral gyrus, activation due to finger and thumb opposition is noted both posterior and lateral to the lesion, with fibers of the corticospinal tract demonstrated medial to the lesion on coronal images.
Image Alignment (Brain)

The Physics of Clinical MR Taught Through Image Alignment

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Third Edition

122 Automatic Image Alignment

An imaging protocol for a given section of the body includes multiple sequences with different contrast weighting (T1, T2, etc.) and orientation (axial, sagittal, coronal, or oblique), each with a given tilt and alignment with respect to specific landmarks. Other factors that may also be optimized include number of slices, FOV, and coverage area. Most practices have established specific imaging protocols for each body part, which are rarely modified depending on the specific clinical question. Standardization of these protocols with different MRI systems and technologies is desired to try and produce uniform imaging sequences for the clinical radiologist. An effective imaging practice strives to obtain high-quality standardized images within an efficient time period.

Automatic image alignment may be performed by the identification of landmarks—for example, the petræa, tibial plateau, or femoral condyles in the knee or femoral heads, greater and lesser trochanter, and hip bone in the hip. The different imaging orientations are then obtained based on predefined field of views and angiograms established in reference to these structures. However, in the head, a different approach is taken.

A nonrigid registration between the individual patient head and a standardized head atlas is performed; clouds of landmarks that were specified in the head atlas are then transformed back into the patient anatomy. Then, the transformed landmarks are used to determine a set of subregion-specific “right” AutoAlign references. Fig. 122.2 shows the first column original uncorrected axial and sagittal images through the brain; the second column shows the corrected localizer information, and the third column shows the final axial T2-weighted and sagittal T1-weighted images obtained.

AutoAlign for the spine is also quite simple as it supports detection of individual vertebral body and disk space alignment. The final slice position results from the application of an additional fitting algorithm, which detects the spine’s geometry. Vertebral disk labeling may also be provided.
Image Alignment (Brain)
Image Alignment (Spine)

Courtesy of Markus Klarhoefer
Image Alignment (Spine)
Simultaneous Multi-slice Echo Planar Imaging ("Multiband")

- Applications include diffusion EPI (brain, spine), DTI, and 3D TOF MRA, T2 TSE

Courtesy of J Richter & M Piccirelli
Recent generation CTs provide substantially greater anatomic coverage, and reduced radiation dose.
Dual energy CT can be used to differentiate between a hematoma and iodine (contrast enhancement) because the attenuation as a function of kV is different for the two.


*Non-contrast, enhanced, & iodine overlay in a hemorrhagic metastasis.*
Identifying Hemorrhage After DSA

- “Contrast material and hemorrhage have similar density on conventional 120-kV CT
- Contrast material hinders interpretation of CT in stroke patients after recanalisation
- Iodine and hemorrhage have different attenuation at lower kVs
- Dual energy CT improves accuracy in early differentiation of hemorrhage and contrast extravasation
- Early differentiation between iodine and hemorrhage helps to initiate therapy promptly”

Identifying Hemorrhage After DSA

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- “DECT is feasible also with a conventional single-source CT machine when equipped with software allowing for sequential data acquisition at the 2 energy levels and a coregistration motion correction algorithm”

“CBV mapping by FPCT is feasible during endovascular stroke treatment … Absolute CBV values of FPCT maps performed immediately following treatment compared well with values from standard PCT maps. Image quality of FPCT was limited but was sufficient to visualize contrast medium extravasation.”

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Flat panel CT

After mechanical recanalization

Courtesy of Neuroradiology, University of Erlangen
Ischemic Infarcts – Detection, Volume Estimation

Objective: Sensitivity of noncontrast computed tomography (NCT) in detecting hyperacute (0–90 minutes) and acute (>90 minutes) cerebral infarction is low. We propose an automatic method to detect and localize ischemic infarcts and to assess its volume from a single NCT scan.

Materials and Methods: The method automatically determines threshold values using regional fluid fluid and white and gray matter, normalizes the brain scan into the left and right hemispheres, and by analyzing histogram attenuation value distributions using parametric difference maps, it detects, localizes, and quantifies the infarct without any segmentation. The method performance was evaluated on 570 patients with clinically confirmed stroke through NCT scans acquired at 3 centers to measure how it matched with that of experts in detection, localization, and assessment of infarct volume. The time from the onset of symptoms ranged from 1.5 to 72 hours for 409 scans and more than 72 hours for 82 scans, with pathologic findings in addition to cerebral infarction; the time was unavailable for 44 scans. In addition, the method was compared with the reference (with 32 scans) and experienced readers’ infarct detection (with 25 × 2 scans) in early ischemic detection (with the time from the onset of symptoms ranging from 1.5 to 7 hours).

Results: The method achieves 99.9% the expert’s infarct detection in hyperacute infarcts, leukoaraiosis cases, and infarct volumes less than 2 cm³ determined by density accuracy radiologists excluded from the analysis. For all cases excluding infarct volumes less than 2 cm³, the method detection accuracy is 93.7%. Overall, the method detection accuracy is 83.2% (early method detection accuracy 93.5%) and 4.9% (nerve detection accuracy 27.8% (25.3%); 37.5% (25-30'); and 57.8% (26-60'); whereas the expert detection accuracy for these cases is 100%. Moreover, the method detected all 21 early infarcts, of which 15 were missed by the stroke experts, and 14 of 15 were missed by a general radiologist. The method performs automatic analysis in approximately 7 seconds.

Conditions: The results demonstrate potential benefits of our method for enhancing expert’s performance because it quickly localizes the infarct and detects cases missed by experts, and it is to be considered an aid in the emergency department because it substantially performs near real time (100% vs. 27%) in infarct detection on NCT.

Key Words: Ischemic stroke, noncontrast computed tomography (NCT); ischemic infarct detection, ischemic infarct localization, ischemic lesion volume from NCT.

Recent advances in diagnostic radiology play a major role in continuously improving clinical practice, including stroke diagnosis and treatment. Stroke is the leading cause of death and is the major cause of permanent disability. The time window to treat stroke is 3 to 4.5 hours for intravenous thrombolysis and 6 hours for intracranial thrombolysis. Noncontrast computed tomography (NCT) remains the first-line diagnosis for emergency evaluation of acute stroke. Computed tomographic (CT) signs of acute ischemic stroke include hypodensity within the infarcted region, obscuration of basal ganglia density, loss of distinction between gray and white matter, pituitary encephalomalacia, narrowing, loss of the subarachnoid, and middle cerebral artery hypodensity, among others. Noncontrast computed tomography; however, suffers from substantial interreader variability in detection and quantification of acute ischemic changes. Moreover, it has poor sensitivity, particularly in the first few hours. Several studies demonstrate infarct detection sensitivity of 30% to 75% within 6 to 8 hours of time window. When compared with magnetic resonance imaging, this sensitivity is only 25% in CT versus 80% in magnetic resonance imaging within the first 3 hours, it is limited to 7% for CT and 46% for MR. Therefore, an automated and rapid detection and localization of ischemic infarcts in NCT would potentially assist in enhancing and expediting scan reading. This is particularly critical in the emergency department (ED), where the scans are frequently reviewed initially by emergency clinicians or even neurologists, neurosurgeons, or radiology residents before being interpreted by expert neuroradiologists.

Computer-assisted approaches can potentially overcome the previously mentioned problems. Computationally, most of CT stroke signs reflect the attenuation value (density) redistribution in the infarcted hemisphere in comparison with the contralateral hemisphere. The stroke-related changes in a single CT image may be subtle to the human eye, especially in the hyperacute stage, but their detailed 3-dimensional (3D) analysis may be sufficient for the computer to detect and localize them.

There are at least 3 advantages of using a computerized approach to automate infarct detection, localization, and quantification in NCT, which may be superior, in certain aspects, over the trained...
“The results demonstrate potential benefits … for enhancing expert’s performance … it quickly localizes the infarct and detects cases missed by experts, and it is to be considered as an aid in the emergency department because it substantially outperforms novice readers (100% vs 27%) in infarct detection.”

Figure 4. Early ischemic changes, first scan and f/u scan, cases missed by the experts
Quantification of Perfusion and Permeability in Multiple Sclerosis

Dynamic Contrast-Enhanced MRI in 3D at 3T

Michael Ingelrath, MSc, Steven Saurbron, PhD, Dominik Marheid, MD, Birgit Erich-Wagner, MD, Tantso Kumpfer, MD, Reinhard Hofield, MD, Maximilian Reiser, MD, and Christian Glasser, MD

Background and Purpose: To quantify cerebrovascular blood flow (CBF), cerebral blood volume (CBV), and blood-brain barrier permeability in multiple sclerosis patients, we aimed to investigate the feasibility of a 3D T1-weighted dynamic contrast-enhanced (DCE-MRI) acquisition in combination with a 2-compartment modeling approach for the quantification of CBF, CBV, and permeability surface area product (PS) in lesions, and normal-appearing white matter (NAWM) in patients with multiple sclerosis (MS).

Material and Methods: In total, 19 MS patients (mean age 35 years, 12 females) underwent DCE-MRI with a 3D T1-weighted spoiled gradient-echo sequence on a 3T MRI scanner. A total of 44 slices (three to five) with an in-plane resolution of 1.7 × 1.7 mm² (matrix size 128 × 1024) were acquired, covering the entire brain. Lesions were identified on T2-weighted and FLAIR images, and the PS was determined on pre-processing steps applied using a 2-compartment model with automated model selection (CFB, CBV, and PS) as a measure of blood-brain barrier leakage area determined in composite-enhancing (CE) and non-enhancing lesions, as well as in NAWM. Perfusion parameters were obtained using the 2-compartment model and automated model selection (CBF, CBV, and PS).

Results: Perfusion quantification produced reasonable values in lesions as well as in NAWM. CBF in lesions, CBV (22.5 (17.1-28.0) vs 15.6 (9.7-21.6) mL/100 mL/min), CBV (1.18 (0.90-1.46) vs 0.96 (0.30-1.39) mL/100 mL/min), and PS (0.90 (0.64-1.32) mL/100 mL/min) were significantly higher in lesions than in NAWM. In non-enhancing lesions, a weakly (r = 0.16) significantly increased CBF of 1.00 (0.25) mL/100 mL/min compared with NAWM was observed.

Comment: Our study demonstrates the feasibility of a 3D T1-weighted DCE-MRI for the quantitative assessment of CBF, CBV, and PS in NAWM as well as in multiple MS lesions scattered throughout the brain, even without previous knowledge of their location. Quantification of the region of interest produces reasonable values both in lesions and in NAWM, but parameter maps would benefit from an increase in contrast-to-noise ratio. The increased values of CBF, CBV, and PS in lesions may reflect inflammatory activity, heterogeneity of parameter estimates suggests a potential for lesion characterization. NAWM appears hypodense, this is in accordance with previous studies, but requires validation with a control group.

Key Words: dynamic contrast-enhanced MRI, 3D, multiple sclerosis, quantification of perfusion

Invest Radiol 2012;47:252-259

Received July 11, 2011, and accepted for publication, after revision, October 5, 2012.

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Invest Radiol 2012;47:252-259

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3D T1-weighted DCE-MRI provides “quantitative assessment of CBF, CBV, and PS in NAWM as well as in MS lesions … Increased values of CBF, CBV, and PS in CE lesions may reflect inflammatory activity … NAWM appears hypoperfused … in accordance with previous studies”

Parameter maps of a single slice. A, Median filtered CBF map, (B) CBV map, (C) PS map, and (D) high resolution contrast-enhanced T1-weighted image.

Invest Radiol 2012;47:252
Evaluation of Iron Content in Human Cerebral Cavernous Malformation Using Quantitative Susceptibility Mapping

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Introduction: The aims of this study were to investigate and validate a quantitative susceptibility mapping (QSM) for iron deposition in cerebral cavernous malformations (CCMs). Materials and Methods: Magnetic resonance imaging (MRI) studies were performed in 15 patients with CCMs using high-resolution 3 T MRI imaging. The QSM analysis was performed using a T2*-weighted gradient echo sequence. The magnetic susceptibility measurements were correlated with iron deposition in vivo using iron-specific susceptibility maps. Results: Quantitative susceptibility mapping successfully detected iron deposition in brain parenchyma and CCMs. The iron concentration was highest in the middle and inferior sections of the CCMs. Conclusions: Quantitative susceptibility mapping is a promising technique for detecting iron deposition in vivo with a high degree of accuracy and reliability. KEY WORDS: quantitative susceptibility mapping, cerebral cavernous malformations, imaging biomarkers, brain iron.

Received for publication November 5, 2013; accepted for publication, after revision, January 9, 2014.

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Iron Content – Quantitative Susceptibility Mapping

Cerebral cavernous malformation (CCM) is a common hereditary vascular anomaly of the brain, presenting in sporadic and familial autosomal dominant forms. Cerebral cavernous malformations affect more than 0.5% of the population, predisposing them to a lifetime risk of stroke and epilepsy related to repeated hemorrhages.1,2 There is currently no therapy to prevent the repeated bleeds in CCM lesions. Previous studies3–5 have reported a significantly increased risk of hemorrhagic transformation in CCM lesions compared with non-CCM lesions, suggesting that CCMs are associated with increased iron deposition in brain parenchyma.6,7 Magnetic resonance imaging (MRI) with T2* and susceptibility weighted imaging (SWI) is a noninvasive technique to detect susceptibility changes.8,9 However, these techniques do not provide a quantification of iron deposition in brain parenchyma or CCMs.8,9

Quantitative susceptibility mapping (QSM) is an emerging technique to quantify iron content in vivo.10,11 QSM has been applied to detect iron deposition in brain lesions caused by multiple sclerosis,12,13 stroke,14 cerebral amyloid angiopathy,15,16 and other neurological disorders.17–20 However, the application of QSM to detect iron deposition in cerebral cavernous malformations has not been reported. The goal of this study was to investigate the feasibility of QSM and our preliminary validation as a biomarker of iron content in CCMs.

MATERIALS AND METHODS

Iron Phantom Preparation

Five phantoms containing various iron concentrations were constructed for validation of QSM acquisition and reconstruction. Each phantom contained 3 Vials with linearly increasing concentrations of iron oxide nanoparticles. Phantom 1 contained iron(III) oxide (ferumoxides) and phantom 2 contained iron(III) oxide (ferumoxides) and iron(III) oxide ( Ferrite).

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The aim of the study was to investigate the feasibility of QSM, with the ultimate goal of monitoring CCM disease progression ... QSM is sensitive to CCM lesions and is feasible for the clinical environment, and QSM values are in the expected range for brain iron.

Hypointensity on SWI is only a qualitative measurement and cannot be used to assess lesion iron content. In distinction, QSM is a quantitative measurement and total susceptibility is directly proportional to the lesion iron content.

Invest Radiol 2014;49:(July)
Quantitative T1 relaxation time maps obtained with MP2RAGE
Additional measurement of quantitative T1 relaxation time maps may provide further potential diagnostic and prognostic information (a) to better discriminate lesion subtypes and (b) to stage and predict the activity and the evolution of MS.
T2* provides information about the structural and chemical compositions of the cortex (myelin, iron), with potential applications for studying myelo- and cyto-architecture.

The future of in vivo Brodmann mapping probably lies in multi-parametric MRI (T1, T2*, and other parameters).
Temporal changes in regional atrophy in a large, relapsing MS cohort

Methods to monitor tissue atrophy may serve as sensitive biomarkers for disease progression and treatment efficacy
Volume-based vs. voxel-based brain morphometry in Alzheimer's disease prediction

- A valuable alternative to quantify brain atrophy and assist in diagnosis

**Introduction:** Volume-based morphometry from conventional T1-weighted images has proved effective to quantify Alzheimer's disease (AD) related brain atrophy and to enable accurate automated classification of AD patients, mild cognitive impairment (MCI), and healthy controls. We aimed to compare these two approaches using the same cohort of patients.

**Materials and Methods:** We conducted a cross-sectional study on 218 participants (143 AD patients, 40 MCI, and 35 healthy controls) from a larger cohort. T1-weighted images were segmented into several brain regions using a fully automated pipeline. Voxel-based and volume-based morphometry were performed using free software tools, then compared using statistical tests.

**Results:** Both methods showed significant differences between AD, MCI, and healthy controls. Voxel-based morphometry revealed more subtle changes, especially in the hippocampus, while volume-based morphometry showed larger, more obvious atrophy in the whole brain.

**Discussion:** Our findings suggest that volume-based morphometry might be more sensitive to early-stage AD changes, whereas voxel-based morphometry could provide more detailed regional information. Further studies are needed to validate these findings and to determine the most appropriate approach for clinical applications.

**Conclusion:** Volume-based and voxel-based morphometry provide complementary insights into AD-related brain atrophy, each with its strengths and limitations. Combining both approaches might offer a more comprehensive understanding of the disease.
Acquisition and post-processing packages are now, and soon to be, available for generation of T1 maps and evaluation of brain morphometry.
Conclusion
Quantitative Imaging in Neuroradiology

• Today
  – Perfusion (CBV, MTT)
    • Ischemia
    • Radiation necrosis
    • Tumor type, grade (diffusion)
  – Hemorrhage vs. iodine
    • Dual energy CT

• Cutting Edge
  – Automated detection and quantification of ischemia
  – Permeability
  – Iron Content

• Active Research
  – T1 mapping
  – T2* mapping
  – Brain morphometry