Computer Aided Diagnosis: Managing the Information Explosion & Decision Making Process – Liver CAD

Jeffrey H. Maki, MD, PhD
University of Washington, Seattle, WA. USA

Goals
1) Become reacquainted with how liver MRI is traditionally performed and interpreted, and the limitations inherent to the technique.
2) Better understand recent developments in software designed to aid in the interpretation, documentation, and reporting of liver lesions – termed “Computer Aided Diagnosis”, or CAD.
3) Explore new directions in liver imaging and how CAD will help us with workflow and to view and interpret the “comprehensive liver exam”.

Introduction
The “traditional” liver MR pulse sequences (T1-weighted, T2-weighted, contrast-enhanced) have been refined and generally standardized over the years, steadfastly making up the mainstay of liver MR since its inception. But the status quo for liver MR is changing, with new pulse sequences such as diffusion-weighted imaging (DWI), MR Elastography (MRE), and quantitative iron and fat determination rapidly finding their way into clinical practice. While all of these techniques are not yet available on all machines, they soon will be, and this will likely change the face of liver MR, adding new functional metrics such as stiffness, fat percentage, mg/g iron, and apparent diffusion value. All of these require a certain amount of preprocessing to display a color-coded image, or churn out a value, most of which is performed on MR consoles or workstations alongside such things as diffusion tensor processing or MRA volume rendering. So certainly one obvious place CAD can play a role is in calculating and presenting these liver-specific metrics to the interpreting imager.

Even with the advent of these elegant new liver techniques aimed somewhat more at diffuse liver disease, the dynamic contrast-enhanced portion of the exam is (and will likely remain) the most efficacious for detecting and classifying focal malignant lesions. We have new contrast agents (hepatobiliary), faster dynamic scans with better fat suppression (parallel imaging, Dixon techniques), better ways to time for peak arterial phase enhancement (e.g. bolustracking); yet despite these advances, we have been interpreting MRI studies in the same manner for years (with the exception of using PACS instead of film). Most radiologists browse through the images/sequences, find abnormalities, correlate these abnormalities across different sequences and comparisons, and then apply training and “experience” to render a diagnosis or differential. The dynamic enhancement properties are usually determined by direct visualization of the gray-scale images, with only occasional use of a quantitative region of interest (ROI) to look at signal intensities. Images and dynamic series are evaluated by scrolling back and forth, and liver and lesion size measurements are manually calculated. In this diagnostic arena that is largely subjective, CAD is poised to play a significant role in changing this perhaps outdated paradigm, providing quantitative tools for more precisely evaluating, measuring, and cataloging lesions.
The role of Liver CAD

One persistent problem with dynamic contrast-enhanced liver MR interpretation is image registration – meaning the liver (and therefore the lesion) are not in the same place on different breath-hold dynamics. This is not simply a matter of the lesion being a slice or two off, but the whole liver and other abdominal contents deforming in a non-linear fashion. This can range from only slightly annoying as one tries to “line” the phases up (which requires time manipulating the PACS), to a real problem when dealing with pre-contrast T1 bright lesions (such as treated HCC) where subtractions are required to see if there is arterial phase enhancement. Luckily, misregistration can be well corrected through computer algorithms built into liver CAD such that the anatomy on each phase is accurately lined up (3D deformable translation). This makes subtractions much more meaningful, eliminating subtraction artifacts that can mimic or hide enhancement (particularly beneficial for treated HCC). It also opens the door to simple (or more complex) ROI analysis to look at quantitative measures of enhancement, relative enhancement etc. with the simple placing of an ROI on a lesion in any image, and then seeing the intensity curve plotted on a graph for immediate visualization.

We have found this graphical information to be extremely helpful in our cirrhotic liver patients. It begs the question of just what exactly “washout” is. Traditionally, “washout” refers to a lesion becoming less dense than the surrounding liver parenchyma during delayed phases. But it is well known the enhancement of background liver on delayed phases is in itself highly variable, ranging from progressive washing out to actually becoming more intense (fibrosis). Thus the “washout” we typically think of depends highly on timing and how the liver is enhancing, whereas the biology is really about what the tumor is doing. Such determinations of absolute (rather than relative) washout are very difficult to make by eye, and are aided greatly by tools that quickly allow such quantitative plots to be made. Again, one place this proves invaluable is in looking at enhancement around TACE or RFA sites – like in breast imaging, progressive increasing enhancement is typically benign, while early enhancement followed by signal decrease is much more indicative of malignancy.

As in breast CAD, it is feasible to color code lesions based on certain characteristics of how they enhance in attempt to draw attention to suspicious lesions. This may be premature at present when we typically have only 4 dynamic phases (pre, arterial portal venous, delay); but another new and exciting research direction involves increasing the temporal resolution of contrast liver examinations to capture a much more dynamic view of how lesions enhance over time. This can, in theory, allow for measuring things like transfer constants, perfusion and blood volume fractions, all of which can be captured, processed and presented using a liver CAD system.

Finally, and perhaps in some ways the most compelling argument to many radiologists, is the ability to standardize and speed up workflow. Just like cardiac MR, where PACS systems are almost always inadequate to adequately visualize what may be a 3000+ image study with CINE clips, multiphase MRA etc, working through the multiple pulse sequences and dynamic phases for a liver MR on a standard PACS system can be incredibly inefficient. A liver CAD system can therefore serve as a platform to present the different sequences in a logical (and customizable) fashion. This is typically done through some amount of pre-processing – a couple of minutes where the software understands what sequence each series
is, performs the proper registration and registered subtractions, calculates things like apparent diffusion coefficient (ADC) values, performs reformats of series (such as axial post contrast to coronal), calculates fat maps etc. This allows for a very complete, very standardized dataset to be produced regardless of the imaging MR unit. Dedicated templates can then be used in order to quickly move between and view different image sets or groups of image sets, with no worry about misregistration. Furthermore, the liver itself can be segmented (for volume etc.) and partitioned into its different Couinaud segments (semi-automated at present). From here lesions of interest can be automatically segmented, sized, and categorized as to Couinaud location (very helpful for standardization in follow-up). The radiologist can then tag each of these lesions with a diagnosis, perhaps including its enhancement curve and/or ADC value, for placement in the report and as reference for future studies. Thus when reading a new study, a quick perusal of the old study tagged and categorized lesions (e.g. each visualized by clicking on a list of lesions) allows one to easily match lesion-for-lesion and describe any progression or updates in diagnosis, speeding up what is often a very cumbersome process in many severely cirrhotic patients.

Summary
Liver MRI is changing, becoming much more complicated – more images, more sequences, more dynamics, new functional techniques. Liver CAD offers the potential to correct for misregistration, streamline liver workflow and reporting, and provide additional tools and processing to aid in the diagnosis of both diffuse and focal liver disease. A comprehensive liver examination, including dynamic contrast-enhanced series as well as functional metrics like elasticity, fat, iron, ADC and perhaps even perfusion are not far off, and will be greatly facilitated by dedicated liver CAD systems.