How to Quantify Hepatic Fibrosis from Different Viewpoints
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Pathologic quantification of hepatic fibrosis

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By means of liver biopsy in cirrhosis, several different kinds of information such as diagnosis of cirrhosis, assessment of cause, fibrosis staging, inflammatory activity and detection of hepatocellular carcinoma can be obtained. Liver biopsy tissue is stained usually by H&E, Masson trichrome and Reticulin for assessment of staging and inflammatory activity.

The histological features of fibrosis development in liver tissue can be different according to causing disease of cirrhosis. In general, it has been known two different histological features of fibrosis development.

Fibrosis starts to develop in portal and periportal area as for viral hepatitis and others, and in perivenular & perisinusoidal area as for nonalcoholic steatohepatitis. Therefore, two different staging system for cirrhosis have been used.

Two major staging system for cirrhosis caused by viral hepatitis and others were proposed by Knodell and Ishak. But the one was too simple and the other was too complicated to apply to practice. For this reason, members of Gastrointestinal Pathology Study Group of Korean Society of Pathologist proposed a staging system in 1999 as follow; stage 1] no fibrosis, stage 2] portal fibrosis, stage 3] septal (bridging) fibrosis, stage 4] cirrhosis. This classification has been used in Korea until now.

The most popular staging system for cirrhosis caused by nonalcoholic fatty liver disease including NASH was proposed by Kleiner at al of the Nonalcoholic Steatohepatitis Clinical Research Network in 2005. Their classification is as follow; Stage 1] Zone 3 perisinusoidal/pericellular fibrosis; (1A] Mild, 1B] Moderate, 1C] Portal/periportal), Stage 2] Zone 3 perisinusoidal/pericellular fibrosis with focal or extensive periportal fibrosis. Stage 3] Zone 3 perisinusoidal/pericellular fibrosis and portal fibrosis with focal or extensive bridging fibrosis. Stage 4] Cirrhosis.

Despite usefulness and subtlety of liver biopsy for cirrhosis staging, it has some limitation also. To make diagnosis, the sample may be sufficiently big, and the nodules sufficiently small. On the other hand a slender core from within a large cirrhotic nodule can be difficult to identify stage. If underestimating the stage of fibrosis is a concern, correlation with clinical and laboratory data helps overcome this problem.

Keywords: Liver, Fibrosis, Stage, Quantification
Assessing the severity of liver fibrosis has direct clinical implications for patient diagnosis and treatment. While liver biopsy is accepted as the gold standard, its result is often disputed due to the sampling error. Furthermore, its clinical utility is often questioned since it is an invasive procedure. Therefore, several imaging-based techniques for staging liver fibrosis have emerged, such as magnetic resonance elastography (MRE) and ultrasound elastography (USE), but they face challenges that include limited availability, high cost, poor patient compliance, low repeatability, and inaccuracy.

Current Computed Tomography (CT) based techniques for liver fat which is one important factor quantify based on the Hounsfield unit (HU) relies on the fact that there is an inverse relationship between liver fat content and liver attenuation. Ultimately, semi-quantitative is remained in nature due to heuristically inferred liver fat concentration.

Dual energy CT (DECT) has been coming under the spotlight again last several years because recent CT systems have gotten an enough ability to apply Dual Energy acquisition for routine clinical use. With the nature of DECT, material quantification is more expected than conventional single energy CT (SECT). The single-source fast kV switching dual-energy method can use spatial and temporal coincident low and high energy data with clinically enough energy separation between two energies. Therefore, more accurate tissue types separation and quantification is expected. One typical imaging method in DECT is material decomposition. This decomposes into specified two materials (material pair) and can scale with the material density by accurate beam hardening correction with the two materials under the projection-space data operation process. In theory, once beam hardening in the two material data (basis pair data) is corrected respectively, these two material density images can be generated, following quantitative imaging and calculation methods such as Monochromatic imaging and Effective-Z calculation can be also generated.

These imaging methods have quantification capability, however liver tissue is composed from several different materials like native tissue, fat, iron, and iodinated contrast material is injected in the multi-phase liver scan, thus two material separation/density images may not be enough for assessing different types of liver tissue.

We therefore developed multi-material decomposition (MMD), a flexible, model-based method that extends DECT’s core material discrimination capability to allow for the disambiguation of a larger number of materials with introducing a biologically driven hypothesis. This calculates multi-material volume fractions for each image pixel based on the response of dual energy images. This method which has great potential for quantitative assessment of the liver fat and fibrosis will be discussed for future clinical application.

**Keywords**: CT, Dual Energy CT, Material Decomposition