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Quantification of liver fat: A comprehensive review

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ABSTRACT

Fat accumulation in the liver causes metabolic diseases such as obesity, hypertension, diabetes or dyslipidemia by affecting insulin resistance, and increasing the risk of cardiac complications and cardiovascular disease mortality. Fatty liver diseases are often reversible in their early stage; therefore, there is a recognized need to detect their presence and to assess its severity to recognize fat-related functional abnormalities in the liver. This is crucial in evaluating living liver donors prior to transplantation because fat content in the liver can change liver regeneration in the recipient and donor. There are several methods to diagnose fatty liver, measure the amount of fat, and to classify and stage liver diseases (e.g. hepatic steatosis, steatohepatitis, fibrosis and cirrhosis): biopsy (the gold-standard procedure), clinical (medical physics based) and image analysis (semi or fully automated approaches). Liver biopsy has many drawbacks: it is invasive, inappropriate for monitoring (i.e., repeated evaluation), and assessment of steatosis is somewhat subjective. Qualitative biomarkers are mostly insufficient for accurate detection since fat has to be quantified by a varying threshold to measure disease severity. Therefore, a quantitative biomarker is required for detection of steatosis, accurate measurement of severity of diseases, clinical decision-making, prognosis and longitudinal monitoring of therapy. This study presents a comprehensive review of both clinical and automated image analysis based approaches to quantify liver fat and evaluate fatty liver diseases from different medical imaging modalities.

Contents

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1. Introduction

Excessive fat accumulation within the liver is called as hepatic steatosis. It has been a prominent feature of some of the most common health problems such as Non-Alcoholic Fatty Liver Disease (NAFLD) and Alcoholic Fatty Liver Disease (AFLD). This study presents a comprehensive review on both clinical and automated image analysis based approaches for quantitative measurement of liver fat and evaluation of fatty liver diseases from different medical imaging modalities.

Patterns of steatosis can be categorized as microvesicular (microsteatosis) and macrovesicular (macrosteatosis) hepatic steatosis [1–5]. Microsteatosis refers to tiny lipid vesicles while macrosteatosis refers to a single large fat vacuole (which is greater than the hepatocyte nucleus) in the cytoplasm of the hepatocytes [6,7]. Microsteatosis is usually more severe than simple steatosis and associated with toxin-induced injury, acute viral and metabolic abnormalities [4]. Macrosteatosis is generally associated with diabetes, dyslipidemia, obesity, alcohol abuse and hyperlipidemia since it affects determination of insulin resistance (i.e.,interfering insulin signaling) and also increases risk of cardiac complications and cardiovascular disease mortality [8–18].

The majority of fatty livers are related to NAFLD (Section 1.1). Both NAFLD and AFLD may continue to damage liver with cell injury and progress to their more aggressive or chronic forms like steatohepatitis, liver failure and even irreversible cirrhosis and HepatoCellular Carcinoma (HCC) [19]. Normal (a), fatty (b, c) and cirrhotic (d) liver tissues are illustrated in Fig. 1.

AFLD and NAFLD are fortunately reversible with timely intervention. Therefore, early and accurate diagnosis is essential. However, accurate diagnosis requires accurate evaluation of fat in the liver using non-invasive, quantitative and reproducible measurements. Accurate evaluation of fat in the liver also plays a vital role prior to transplant [20] since even a mild degree of steatosis in a donor liver could potentially increase the chance of liver failure in the recipient and can increase morbidity for the donor as well [7,21–23]. Clinical researchers reported severity of steatosis (when it is greater than 66%) as exclusion criteria for patients who need liver resection due to expected high risk of post-operative complications [22,24]. Due to the growing demands of the organ and the shortage of the available cadaveric organ, steatotic liver grafts are currently the most prominent “extended criteria” organs [20,25].

Studies in the literature (see Section 3) indicate a growing interest in methods for accurate and quantitative grading of fat in the liver, motivated by an increasing need for early diagnosis, treatment and also monitoring of fatty liver diseases (see Sections 2 and 3).

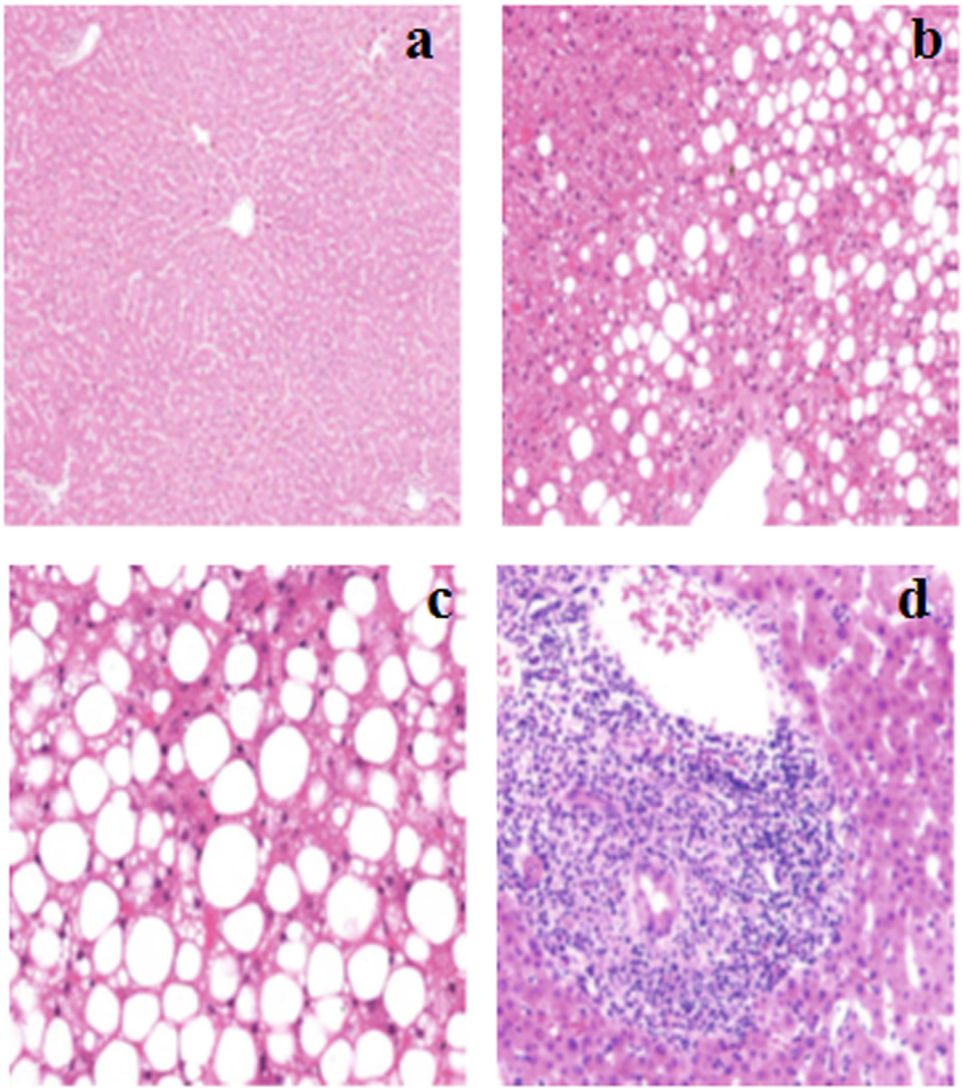

Fig. 1. Histological slides show a normal liver tissue (a), fatty liver tissue (AFLD) (b), NAFLD (c)) and cirrhotic form of a liver tissue (d) [19].