Computerized Medical Imaging and Graphics 38 (2014) 104–112

Contents lists available at ScienceDirect

Computerized Medical Imaging and Graphics

journal homepage: www.elsevier.com/locate/compmedimag

Hunting for necrosis in the shadows of intravascular ultrasound

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ARTICLE INFO

Article history:
Received 5 October 2012
Received in revised form 17 July 2013
Accepted 19 August 2013

Keywords:
Intravascular ultrasound
Tissue characterization
Nakagami distribution
Ultrasound signal confidence
Machine learning
Atherosclerosis
Necrotic core

ABSTRACT

Coronary artery disease leads to failure of coronary circulation secondary to accumulation of atherosclerotic plaques. In adjunction to primary imaging of such vascular plaques using coronary angiography or alternatively magnetic resonance imaging, intravascular ultrasound (IVUS) is used predominantly for diagnosis and reporting of their vulnerability. In addition to plaque burden estimation, necrosis detection is an important aspect in reporting of IVUS. Since necrotic regions generally appear as hypoechic, with speckle appearance in these regions resembling true shadows or severe signal dropout regions, it contributes to variability in diagnosis. This dilemma in clinical assessment of necrosis imaged with IVUS is addressed in this work. In our approach, fidelity of the backscattered ultrasonic signal received by the imaging transducer is initially estimated. This is followed by identification of true necrosis using statistical physics of ultrasonic backscattering. A random forest machine learning framework is used for the purpose of learning the parameter space defining ultrasonic backscattering distributions related to necrotic regions and discriminating it from non-necrotic shadows. Evidence of hunting down true necrosis in shadows of intravascular ultrasound is presented with *ex vivo* experiments along with cross-validation using ground truth obtained from histology. Nevertheless, in some rare cases necrosis is marginally overestimated, primarily on account of non-reliable statistics estimation. This limitation is due to sparse spatial sampling between neighboring scan-lines at location far from the transducer. We suggest considering the geometrical location of detected necrosis together with estimated signal confidence during clinical decision making in view of such limitation.

1. Introduction

Intravascular ultrasound (IVUS) is a predominant adjunct imaging modality for diagnosis and reporting of vulnerable vascular plaques during percutaneous coronary interventions (PCI). Although there exist other non-invasive or minimally invasive imaging modalities like intravascular optical coherence tomography (OCT) [1], intravascular near-infrared spectroscopy (NIR) [2] adjunct to primary imaging using computed tomography angiography (CTA) [3] or magnetic resonance imaging (MRI) [4], IVUS is preferred for its multifaceted benefits. A major benefit is its high depth of field and ability to characterize tissue heterogeneity in a plaque towards indicating vulnerability [5,6].

Histological examination reveal plaques to non-exclusively constitute of fibrotic, lipidic and calcified lesions; with their independent or joint existence conveying separate diagnostic relevance [7]. Each type of tissue is characterized by a family of scatterers which backscatter ultrasonic acoustic pulse resulting in the echo used for ultrasonic imaging [8]. The multi-scalar co-localized heterogeneity of biological tissues and their stringent spatial/spectral response to ultrasonic signals, results in formation of heterogeneous speckle patterns in a B-mode IVUS image. Such heterogeneous speckle patterns subjectively affect image interpretation and diagnostic reporting [9]. There exist ambiguities related to vulnerability assessment; like relative presence

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http://dx.doi.org/10.1016/j.compmedimag.2013.08.002

of lipidic and fibrotic tissues, their heterogeneity, distinction of dense fibrotic from calcified masses visible as hyperechoic region in IVUS. However, a major clinical challenge is find indications of vulnerable plaques, primarily indicated by presence of necrosis [10]. Its hypoechoic appearance in IVUS complicates diagnosis and is often ambiguously associated with post-calcification shadowing or severe signal attenuation [11,12].

Signal processing and machine learning techniques have been employed since the past decade to characterize heterogeneous tissues imaged with IVUS, with the objective to assist plaque vulnerability assessment. Popular techniques employ integrated backscatter coefficients [13] computed from the ultrasonic echo (RF data) [14]; spectral- and texture-driven methods [8,15,16]; mixture model speckle density estimation techniques [17] and differential echogenicity measurement [18]. Commercially available tissue characterization software have been implemented for the clinical IVUS scanners both from Volcano Therapeutics (Virtual Histology), Boston Scientific (iMap) [19] and Terumo (IB-IVUS). Different corelab software packages offer advance image analysis and quantification of the results, including automatic borders or exclusion of wire artifacts (QIvus,[1] EchoPlaque[2]). Clinical studies with such tissue characterization techniques have indicated their inability to identify nature of tissues in hypoechic regions, often systematically misclassified to be necrotic, resulting in overemphasis of plaque vulnerability [8,9,11,12,20].

Hypoechogenity in IVUS can be associated with either of (a) shadowing behind strong calcification [12], (b) severe signal dropout [9,11], and (c) lack of scattering from necrotic areas [11]. Diagnostically it is relevant to detect true necrosis in hypoechoic regions and discriminate it from shadowing or severe signal dropout, for assessing plaque vulnerability [7,10]. In this work our objective is to *hunt down* (detect) true necrotic areas in the plaque imaged in IVUS. According to proposition in [11], the intuitive approach would be to identify low confidence samples in the received ultrasonic backscattered signal, and then characterize the statistical physics model from which these signals originate, to indirectly identify the speckle model for necrotic tissue, while directly discriminating true necrosis from signal dropout or acoustic shadowing. Fig. 1 illustrates an IVUS image of an atherosclerotic plaque with heterogeneous composition of nectoric areas and shadowing due to signal dropout. The necrotic cores are histologically correlated with Hematoxylin and Eosin (H&E) stained section [21] and consists of both early and late necrosis. In this paper, our objective is to identify elusive late necrotic regions in plaques and Fig. 1(d) illustrates the *hunted down* true necrosis in shadows of IVUS.

In this paper we present a framework for achieving our objective of detecting true necrosis by jointly learning backscattered ultrasonic signal confidence [22,23] and statistical properties of ultrasonic speckles [24] corresponding to tissues constituting the plaque. These metrics used here are directly estimated using the envelope of RF data. A random forest [25,26] ensemble learner is employed for the purpose of learning this heterogeneous space of ultrasonic signal confidence and speckle statistics. The rest of the paper is organized accordingly: Section 2 presents details of the framework. Section 3 presents experimental evaluation of the proposed method and performance comparison through histological cross-validation. Finally the work is concluded in Section 4 with a brief note on possibility to leverage this framework for solving such complex and heterogeneous tissue identification problems in ultrasonic imaging.

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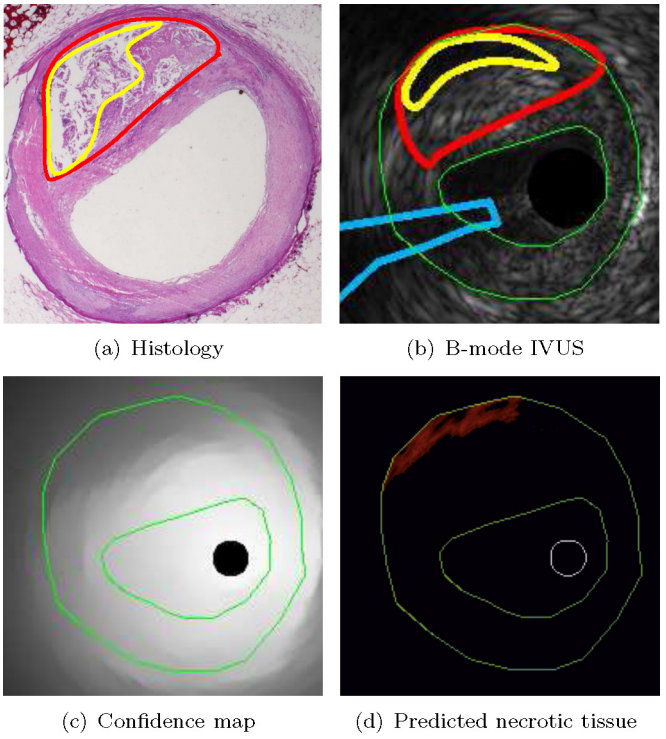

Fig. 1. Illustration of hypoechoic regions in IVUS and associated histological correlation. (a) H&E stained histology of the tissue section corresponding to the (b) B-mode IVUS image with the plaque boundary traced in green contour. The necrotic region with heterogeneous tissues is marked in red contour, late necrotic region characterized by hypoechoic region in the IVUS is marked in yellow colour, shadowing due to signal dropout at the guide-wire location is marked in blue. (c) Signal confidence estimated for this acquisition. (d) Necrotic tissue estimated by our approach and marked in red. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

2. Learning of ultrasonic statistical physics for true necrosis detection

Ultrasonic acoustic pulse travelling through tissues is partly backscattered, attenuated, or absorbed. The backscattered acoustic pulse contributes to the returned echo used for ultrasonic imaging. Backscattering of these pulses is generally caused by scatterers present in the media through which the ultrasonic acoustic pulse propagates. Contribution of these scatterers is generally treated as a random walk on account of their random location within the resolution limit of range cell of the propagating ultrasonic pulse [24,27].

The probability $p(y|r)$ that a sample of received ultrasonic echo signal r characterizes a tissue of type $y \in \mathcal{Y}$ can be represented in the Bayesian paradigm as

$$p(y|r) = \frac{p(r|y)P(y)}{p(r)} \tag{1}$$

where $p(r|y)$ is the conditional likelihood of received ultrasonic echo signal r known *a priori* for tissue of type y, $P(y)$ is the prior probability of tissue of type y, and $p(r)$ is total likelihood of r. Our objective being to *hunt down* true necrosis, often ambiguously associated with shadows, the two classes of tissues considered here are $\mathcal{Y} = \{\text{necrosis, non} - \text{necrotic tissue}\}$. The conditional likelihood $p(r|y)$ is a function of these tissue specific effects on ultrasonic signals: (a) confidence of the received ultrasonic signal $f_1(r; \ldots|y)$ and (b) statistics of received ultrasonic signal $f_2(r; \ldots|y)$.