Computers in Biology and Medicine 80 (2017) 77–96

Contents lists available at ScienceDirect

Computers in Biology and Medicine

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

Stroke Risk Stratification and its Validation using Ultrasonic Echolucent Carotid Wall Plaque Morphology: A Machine Learning Paradigm

Tadashi Araki[a], Pankaj K. Jain[b], Harman S. Suri[c], Narendra D. Londhe[d], Nobutaka Ikeda[e], Ayman El-Baz[f], Vimal K. Shrivastava[d], Luca Saba[g], Andrew Nicolaides[h,i], Shoaib Shafique[j], John R. Laird[k], Ajay Gupta[l], Jasjit S. Suri[b,c,m,*]

[a] *Division of Cardiovascular Medicine, Toho University Ohashi Medical Center, Tokyo, Japan*
[b] *Point-of-Care Devices, Global Biomedical Technologies, Inc., Roseville, CA, USA*
[c] *Monitoring and Diagnostic Division, AtheroPoint™, Roseville, CA, USA*
[d] *Department of Electrical Engineering, NIT Raipur, Chhattisgarh, India*
[e] *Cardiovascular Medicine, National Center for Global Health and Medicine, Tokyo, Japan*
[f] *Department of Bioengineering, University of Louisville, USA*
[g] *Department of Radiology, University of Cagliari, Italy*
[h] *Vascular Screening and Diagnostic Centre, London, England*
[i] *Vascular Diagnostic Centre, University of Cyprus, Nicosia, Cyprus*
[j] *CorVasc Vascular Laboratory, 8433 Harcourt Rd #100, Indianapolis, IN, USA*
[k] *UC Davis Vascular Centre, University of California, Davis, CA, USA*
[l] *Brain and Mind Research Institute and Department of Radiology, Weill Cornell Medical College, NY, USA*
[m] *Department of Electrical Engineering, University of Idaho (Affl.), ID, USA*

ARTICLE INFO

Keywords:
Stroke
Carotid wall
Ultrasound
Near
Far
Segmentation
Machine learning
Precision of merit
ROC

ABSTRACT

Stroke risk stratification based on grayscale morphology of the ultrasound carotid wall has recently been shown to have a promise in classification of high risk versus low risk plaque or symptomatic versus asymptomatic plaques. In previous studies, this stratification has been mainly based on analysis of the far wall of the carotid artery. Due to the multifocal nature of atherosclerotic disease, the plaque growth is not restricted to the far wall alone. This paper presents a new approach for stroke risk assessment by integrating assessment of both the near and far walls of the carotid artery using grayscale morphology of the plaque. Further, this paper presents a scientific validation system for stroke risk assessment. Both these innovations have never been presented before.

The methodology consists of an automated segmentation system of the near wall and far wall regions in grayscale carotid B-mode ultrasound scans. Sixteen grayscale texture features are computed, and fed into the machine learning system. The training system utilizes the lumen diameter to create ground truth labels for the stratification of stroke risk. The cross-validation procedure is adapted in order to obtain the machine learning testing classification accuracy through the use of three sets of partition protocols: (5, 10, and Jack Knife).

The mean classification accuracy over all the sets of partition protocols for the automated system in the far and near walls is 95.08% and 93.47%, respectively. The corresponding accuracies for the manual system are 94.06% and 92.02%, respectively. The precision of merit of the automated machine learning system when compared against manual risk assessment system are 98.05% and 97.53% for the far and near walls, respectively. The ROC of the risk assessment system for the far and near walls is close to 1.0 demonstrating high accuracy.

1. Introduction

Stroke is the fifth leading cause of death in United States. On an average, someone in the United States has a stroke every 40 s [1]. The WHO estimates that these Cerebrovascular accidents (CVA), or strokes account for the loss of 6.7 million lives per year [2]. One of the leading cause of these strokes is carotid artery disease (CAD) [3–5], which occurs when the carotid arteries gets blocked (so called "stenosis"). When carotid artery stenosis occurs, there is a risk that oxygenated blood may not be available to the brain because of either reduced

* Correspondence to: Monitoring and Diagnostic Division, AtheroPoint™, Roseville, CA, USA.
E-mail address: Jasjit.Suri@atheropoint.com (J.S. Suri).

http://dx.doi.org/10.1016/j.compbiomed.2016.11.011
Received 9 October 2016; Received in revised form 20 November 2016; Accepted 25 November 2016
0010-4825/

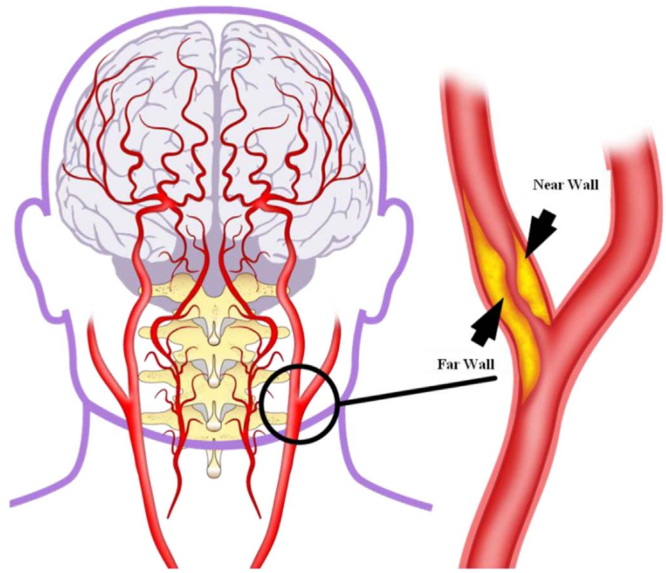

Fig. 1. Carotid anatomy (left) and carotid atherosclerotic plaque formation in near and far walls (right).

perfusion pressure from the narrowed carotid artery or because of a rupture plaque that blocks a downstream blood vessel in the brain. This stenosis of the carotid arteries as depicted in Fig. 1 is most commonly caused by atherosclerosis [6]. Atherosclerosis is caused due to the accumulation of fatty deposits known as plaque along the innermost layer of the arteries (causing stenosis), where blood normally flows.

1.1. Small changes in wall leading to cIMT

The biology of atherosclerotic disease leads to the formation of different plaque components in the carotid arterial wall over time [6]. The atherosclerotic plaque has multiple components such as plaque hemorrhage (PH), thrombus (T), lipids, necrotic cap thickness (NCT), intima thickness, calcium, fibrosis cap (FC) and smooth muscle cells (SMCs). [7,8]. There are two biological changes erupting out of this formation: (a) small changes in intima and media walls [9] and (b) aggressive changes in the arterial wall leading to stenosis [10]. These small changes in the walls of the carotid artery bring in an increase in thickness, which is measured as the carotid intima-media thickness (*c*IMT). Scientists have used *c*IMT as a biomarker for predicting the occurrence of major adverse cardiovascular events [11,12]. Several studies have shown a relationship between varying *c*IMT thresholds and cardiovascular disease (CVD) [13–16]: (*c*IMT >0.8 mm) [10], (*c*IMT >0.9 mm) [13,15], (*c*IMT >1.1 mm) [17], (*c*IMT >1.15 mm) [18], and (*c*IMT >1.26 mm) [19].

1.2. Role of lumen diameter

On the other hand, multifocal and aggressive changes in the arterial wall cause a drastic change in lumen diameter (LD), and are referred to as stenosis. Previous research [12,20] has shown a link between LD and CVE. Polak et al. 2011 in reference [21] hypothesized that an increase in the internal diameter of common carotid artery (CCA) which is also known as the LD, is associated with age, gender, and echocardiographically estimated left ventricular (LV) mass. Recent studies have shown that the carotid arterial diameters also have a better predictive power for CAD [11,12,22–24]. We infer that LD offers a method for characterization of high and low stroke risk [25–28]. This is important to note here that these measurements are important and must be calculated without subjectivity and further can be utilized as a building block for risk assessment based on machine learning.

1.3. Role of grayscale morphological-based tissue characterization

As plaque matures with age in a carotid artery, the number of plaque components increases in the plaque [29]. This is shown to change the echolucency in ultrasound scans [30]. These plaques can be symptomatic or asymptomatic [31–33]. In general, studies have shown that symptomatic plaques may be predominantly hypo-echoic in nature, while the asymptomatic plaques are less bright and relatively hyper-echoic, though there is significant variability across individual patients [30]. Due to multifocal nature of the disease, it has been seen that hypo-echoic plaque regions can be surrounded by the hyper-echoic regions [34]. It is therefore challenging to characterize the plaque visually and thus, it is necessary to have a morphological-based tissue characterization protocol for stroke risk assessment. We assume that the plaque components in ultrasound scans can be used to assess the risk based on tissue morphology along with the carotid LD measurements which can act as a label for high or low risk. This can be accomplished using machine learning and this study adapts such a model. In order to classify the risk posed by different levels of plaque buildup in the carotid artery, a technique of tissue characterization is used, which qualitatively analyzes the different statistical features that compose the plaque in the carotid artery [35–39]. Note that the risk assessment based alone on LD is not sufficient. This is because the grayscale information corresponding to different plaques (such as: lipids, macrophages, fibro fatty and calcium) in the wall region is not utilized during the risk assessment [40–42].

1.4. Importance of near wall and tissue characterization

The study of ultrasound tissue characterization relies on the results from B-mode ultrasound [9] in order to characterize the difference between high and low risk patients based on the values of the statistical features [43]. This process is repeated in the near wall, far wall, and combined wall of the carotid artery in order to determine a holistic method of risk assessment while at the same time comparing the error obtained from two different places of interaction within an ultrasound image. This is of unique value because the near wall of the carotid artery is historically thought to be of little importance [14] to the idea of risk assessment and is thus the main contribution of this study. The reason for this is the low intensity contained in ultrasound images corresponding to the near wall. However, as there is equal likelihood for the development of plaque buildup on this side of the carotid artery, this current study aims to develop a machine learning based stroke risk assessment system (sRAS) so that, the visual (manual) error from the low intensity of the near wall does not affect the reliability of the overall results.

1.5. sRAS for near and far walls using machine learning paradigm

The machine learning approach [40] adapted in this study aims to provide a more comprehensive solution to the problems in manual risk assessment, especially when the combined grayscale wall (near and far) of the carotid artery ultrasound scan is taken into consideration. By first segmenting the desired wall region in ultrasound scans, extract its grayscale features, along with measurement of LD, we were able to train the machine learning system and obtain the high and low risk coefficients [44]. This information was then given to the system along