Review

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The Journey of Elastography: Background, Current Status, and Future Possibilities in Breast Cancer Diagnosis

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Abstract

Elastography is a promising way to assess tissue differences regarding stiffness or elasticity for what was historically assessed manually by palpation. Combined with conventional imaging modalities (eg, ultrasonography [US]), elastography can potentially evaluate the stiffness of a breast lesion and consequently help to detect malignant breast tumor from benign ones. Recent studies show that ultrasonographic elastography (USE) provides higher image quality compared with conventional B-mode US or mammography during breast cancer diagnosis, which eventually helps to reduce false-positive results (ie, increased specificity) and therefore is useful in avoiding breast biopsy. This article reviews the basics of elastography technique, classifications, diagnosis results obtained from clinical studies to date for differentiating malignant breast tumors from benign lesions, and its future possibilities. In addition, this article generalizes different elastography methods, modes, and associated imaging modalities in a simpler way and attempts to identify misconceptions and confusion related to existing elastography techniques. It also makes an effort to identify the gaps of information that need to be filled so that interested researchers can get an overall idea of elastography-based methods in a convenient way to carry out their research on breast elastography for prospective future applications, eg, breast cancer diagnosis or even in intraoperative breast tumor localization.

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Introduction

Breast cancer is one of the most common malignancies in women and the second primary cause of cancer-related death.[1] The hope is that if diagnosed at a very early stage, breast cancer can be completely cured. Because of the absence of a known preventable reason for breast cancer, the most essential factor to lessen the mortality rate and the extent of treatment required is detection at an early stage through screening. Because of advanced screening facilities, thousands of women are diagnosed with breast cancer at an early stage every year, even before they start to feel a lump (ie, impalpable lesions). However, the scenario is relatively different in developing countries. Because of the high cost of screening tests, many women cannot afford regular screening, which leads to them dying, because from the time the tumor is detected/diagnosed or the surgery is performed, the root of the cancer has spread much deeper. Apart from cost-effectiveness, there are some other drawbacks of existing screening tools. Because of the sophisticated operation and the need for highly skilled technicians to operate, not every country can afford such systems because they lack technically skilled surgeons. In addition, the conflict of sensitivity versus specificity also matters. Most of the current methods are highly sensitive yet lack specificity, resulting in an alarming number of false-positive cases. Consequently, the increased false-positive results also increase the rate of unnecessary biopsies. Some methods even fail to diagnose millimeter-sized or cellular-level cancers. As a result, despite having regular screening tests, breast cancers can fail to be diagnosed at an early curable stage. Surprisingly, these are scenarios from developed countries, not to mention developing ones. In any of the cases, it is troublesome for patients. Therefore, the desire for the development of a single suitable screening test for breast cancer is inevitable, ie, 1 that will be highly sensitive as well as specific,

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easily performed, and cost-effective without the need for a special hardware setup so that the entire world can reap the benefits from it, regardless of race or continent or economical, developmental, or educational solvency. After analyzing these criteria, elastography seems to be 1 of the promising candidates in this regard. Because of the attractive features of elastography as a potential breast cancer diagnostic tool, research on elastography for breast cancer diagnosis has shown an increasingly exponential trend since 2000 until the present (Figure 1). It is important to note that the study of elastography began almost 2 decades ago, but from the beginning of the 21st century, it has emerged significantly with several published articles in peer- reviewed journals. Hence, we have considered articles published since 2000 for this review.

The standard diagnostic process for breast cancer is often termed the *triple assessment* and has 3 stages: *clinical examination, imaging*, and *needle biopsy*. The first stage involves a medical history and clinical examination, followed in the second stage by imaging of the breast using either ultrasonography (US) or mammography, and finally in the last stage laboratory testing of the sample breast tissue obtained using a needle biopsy procedure. Although mammography and US are the 2 most popular imaging methods in the second stage of the diagnostic process, both methods have some limitations.[2] As reported by Saarenmaa et al[3], mammography applied in dense breast may sometimes result in false-negative results, whereas US has poor specificity because most stiff lesions turn out to be benign. Therefore, breast elastography has been introduced to overcome these limitations and to provide a better breast image for lesion characterization.[4-11] Besides, breast elastography can act as a bridge between stage 2 and stage 3 of triple assessment of breast cancer and eventually helps to reduce the number of unnecessary biopsies.

Regardless of the fact that the study of elastography has been ongoing for > 2 decades, most studies were performed almost behind a closed door. Therefore, after 2 decades of elastography research worldwide, there is a thin connection between research groups. For example, the current elastographic techniques developed in research laboratories that have already started appearing in the market are most likely not quantitatively or operator independent. In other words, there are no universal standards for scoring and terminology. Therefore, the term *elastography* can cover very different physical phenomena. Although there are few elastography machines by different manufacturers available, there is still a significant amount of confusion, misconception, and lack of clarity about the concept of elastography, its implementation, and its interpretation for breast tumor assessment.

The purpose of this article is to point out the commonly encountered confusion and misconceptions and correlate all the existing methods and classification techniques to provide a better, broader, and clearer view to the interested researchers and, of course, to open the window of elastography widely for the research community. It is high time to understand the underlying mechanisms of different elastographic techniques properly to make the best use of it in wide clinical practice.

Elastography

Basic Principle

The concept of elastography was first introduced after 1990[12] and started to be used in the clinical setting in 1997.[13] Elastography is a noninvasive imaging technique in which the local tissue strains are measured directly (eg, the strain ratio/the Young modulus) or indirectly (eg, shear-wave velocity) after external stress (static or dynamic) is applied to perturb/compress the tissue. The tissue stiffness can be measured with elastography using a 3-step process[14]:

- Apply a small stress to the tissue.
- Measure the tissue displacement.
- Calculate stiffness based on the tissue displacement.

Figure 1 **Trend of Elastography Research Works Published in Major Journals Indexed by PubMed From 2000 to the Present**