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Magnetic resonance elastography (MRE) in cancer: Technique, analysis, and applications

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ABSTRACT

Tissue mechanical properties are significantly altered with the development of cancer. Magnetic resonance elastography (MRE) is a noninvasive technique capable of quantifying tissue mechanical properties in vivo. This review describes the basic principles of MRE and introduces some of the many promising MRE methods that have been developed for the detection and characterization of cancer, evaluation of response to therapy, and investigation of the underlying mechanical mechanisms associated with malignancy.

Contents

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1. Backgound

1.1. Introduction

It has been understood for several millennia that many physiological and pathological processes cause marked changes in the mechanical properties of tissue [1]. Physicians utilize touch to detect and diagnose abnormalities, notably cancer. Palpation contributes significantly to cancer detection as evidenced by the promotion and wide use of self-breast exams to monitor for the presence of disease [2]. While palpation is an incredibly powerful diagnostic tool, it is qualitative and limited by the sensitivity and experience of the practitioner. Additionally, unless it is combined with surgery, palpation can only be used to assess superficial pathologies.

In the past two decades a new, noninvasive imaging technique known as magnetic resonance elastography (MRE) has been developed to spatially resolve the mechanical properties of soft tissues [3]. MRE is particularly well suited for the study of cancer; the mechanical properties of tumors have implications for detection, characterization, prediction of response to treatment, and monitoring of therapy response. This review describes the basic principles of MRE, including the underlying physiological basis, data acquisition and analysis, limitations, and current clinical applications in cancer.

1.2. Clinical significance

Imaging plays a central role in oncology. Imaging is used not only for cancer screening, but also for diagnosis and staging, guiding cancer treatments, determining response to therapy, and monitoring for cancer recurrence. MR imaging techniques are broadly recognized as powerful and versatile tools for the noninvasive assessment of cancer morphology and functionality. However, even with the most advanced imaging techniques, significant needs remain, especially in the realm of oncology.

MR techniques are highly sensitive for the detection of cancer, but typically have low specificity for determination of tumor grade and malignant vs. benign status. Current clinical techniques employed in oncology use many different types of MR contrast. Dynamic contrast-enhanced MR (DCE-MRI) utilizes exogenous contrast agents (low molecular weight gadolinium chelates) administered in the blood stream that shortens the T_1 relaxation of blood, making it appear brighter on T_1-weighted MR images. The clinical application of DCE-MRI is to assess tumor angiogenesis, vascular permeability, and blood flow, based on the fact that tumor vessels are generally more permeable, heterogeneous in size, and tortuous than normal vessels. Diffusion-weighted imaging (DWI) employs the diffusivity of water as a quantitative parameter which reflects the diffusion of water molecules in tissue. A hallmark of cancer is increased cellularity and vascularity, both of which restrict diffusion resulting in lower apparent diffusion coefficient (ADC) values. Recent studies suggest that DWI may be sensitive to extracellular fibrosis, shape and size of the intercellular space, and other microscopic organization of tumor [4]. DWI has been used for tumor detection and characterization and for predicting and monitoring response to therapy. MR spectroscopic imaging (MRSI) is a technique that images tumor metabolic markers for cancer diagnosis, metabolic phenotyping, and characterization of the tumor microenvironment. The major limitation of MRSI is low spatial and temporal resolution due to low tissue concentrations of metabolites in tissue. An emerging tool in oncologic imaging is multiparametric MRI (MPMRI); the combination of conventional anatomical MRI and functional techniques. MPMRI improves the accuracy for identification, staging, and treatment planning in prostate cancer [5].

There is a clinical need for noninvasive imaging techniques for the accurate diagnosis and monitoring of cancer. The director of the National Cancer Institute and Nobel laureate Harold Varmus, M.D. has stated that "There is a tremendous need to incentivize development of validated and accepted diagnostics in order to keep pace with the explosion of new, targeted cancer drugs that are in the pipeline" [6]. MRE as a technique can provide contrast between the mechanical properties of normal and diseased tissue has the potential of playing an important role in the study and treatment of cancer.

2. Fundamentals of magnetic resonance elastography

Since the first publication in 1995 by Muthupillai et al. [3] which described a novel technique of imaging the propagation of mechanical waves in a gel phantom, MRE has been used to noninvasively quantify the mechanical properties of liver, brain, breast, heart, lung, spleen, kidneys, pancreas, uterus, muscle, and thyroid [7–19]. Clinically, MRE is routinely used for the noninvasive assessment of liver fibrosis and has replaced biopsy as the standard of care at the Mayo Clinic since 2007 [20]. The term 'elastography' was first introduced in 1991 to describe an ultrasound-based technique to determine a qualitative description of tissue strain resulting from external compression [21]. Elastography exists across several modalities including MR, ultrasound, optical imaging, and mechanical testing; however, an extensive description of each technique is outside the scope of this review.