Biomaterials 33 (2012) 5124–5129

Contents lists available at SciVerse ScienceDirect

Biomaterials

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

Hollow silica and silica-boron nano/microparticles for contrast-enhanced ultrasound to detect small tumors

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ARTICLE INFO

Article history:
Received 24 February 2012
Accepted 18 March 2012
Available online 11 April 2012

Keywords:
Ultrasound
Nano
Silica
Shells
Imaging
Contrast

ABSTRACT

Diagnosing tumors at an early stage when they are easily curable and may not require systemic chemotherapy remains a challenge to clinicians. In order to improve early cancer detection, gas filled hollow boron-doped silica particles have been developed, which can be used for ultrasound-guided breast conservation therapy. The particles are synthesized using a polystyrene template and subsequently calcinated to create hollow, rigid nanoporous microspheres. The microshells are filled with perfluoropentane vapor. Studies were performed in phantoms to optimize particle concentration, injection dose, and the ultrasound settings such as pulse frequency and mechanical index. *In vitro* studies have shown that these particles can be continuously imaged by US up to 48 min and their signal lifetime persisted for 5 days. These particles could potentially be given by intravenous injection and, in conjunction with contrast-enhanced ultrasound, be utilized as a screening tool to detect smaller breast cancers before they are detectible by traditional mammography.

1. Introduction

Excising non-palpable breast cancers in breast conservation therapy is difficult because surgeons must rely on mammographic localization. Wire localization has been the standard method to localize non-palpable tumors, but the reported positive margin rate from wire-localized excisions of breast cancers is approximately 20–50% [1–3]. This poor performance is partly due to wire movement during patient transport to the operating room as well as manipulation during surgery which results in positive margins with wire localization. Radioactive seeds have also been used for breast conservation therapy with a substantial improvement in performance relative to guide wires [4,5]. Unfortunately, these seeds are rarely used due to short radioactive half-life and the need to expose both the patient and the operating room personal to radiation. Our proposed method of localizing tumors with nanoparticles detectable with ultrasound (US) has two main advantages: no radiation risk, and it allows for multiple injections to better outline the tumor and its margin for the surgeon to reorient during surgery to ensure complete tumor removal. A recent survey study of breast surgeons practicing in community hospital settings has shown that at least one third are already routinely using intraoperative US [6]. Therefore a new technology that improves US performance could not only replace an older technique that utilizes radioactivity, but could also be readily implemented by clinicians.

Mammographic screening has been shown to decrease mortality rates by 15–25% in several large randomized prospective studies, however, mammographic sensitivity is impaired for non-calcified masses in radiographically dense breast tissue [7]. This data suggests that further improvement in screening accuracy could increase survival. In North America, breast US is most often a targeted examination, limited to the area of concern based on palpation or mammography. MRI has been extremely beneficial for

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doi:10.1016/j.biomaterials.2012.03.066