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Research paper

Comparative biomechanical study of using decellularized human adipose tissues for post-mastectomy and post-lumpectomy breast reconstruction

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ABSTRACT

Developing suitable biomaterials for post-mastectomy or post-lumpectomy breast reconstruction is highly important. This study is aimed at evaluating biomechanical suitability of decellularized adipose tissue (DAT) for this purpose. The study involves computational experiments for evaluating deformation of the breast reconstructed using DAT under loading conditions pertaining to two common body position changes of prone-to-supine and prone-to-upright. This was conducted using nonlinear finite element models where the breast geometry was obtained from MRI image of a female breast. The experiments were performed using DAT sourced from various adipose tissue depots in comparison to natural adipose tissue. Data obtained from the conducted experiments showed no contour defects with various DAT materials for simulated post-mastectomy or post-lumpectomy breast reconstruction under the loading conditions. They also demonstrated that a breast reconstructed using DAT derived from the breast or subcutaneous abdominal depots exhibit significantly closer deformation, both qualitatively and quantitatively, to that of a normal breast under the same loading conditions. Similarity of DAT deformation to that of natural breast tissue in post-surgery breast reconstruction was assessed using nonlinear finite element analysis. Our results provide evidence that DAT derived from subcutaneous abdominal and breast depots yield more analogous deformation pattern to the natural tissue in post-mastectomy breast reconstruction applications. This is quite encouraging, as breast and subcutaneous adipose tissue can be readily obtained in large quantities from

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breast or abdominal lipo-reduction surgery procedures. Furthermore, in post-lumpectomy cases all DAT samples used in this research showed similar deformation, and thus are suitable as breast tissue substituents.

1. Introduction

Breast cancer is the second most prevalent cancer among women, affecting one in every eight women during the course of their lifetime (American Cancer Society, 2014). The majority of breast cancer patients are treated surgically, undergoing either lumpectomy or mastectomy in order to combat the disease. Lumpectomy involves the removal of the tumor and a small amount of surrounding normal tissue, while mastectomy involves total removal of the affected breast. Breast tumor excision often results in contour defects. In addition to changing the patient's physical appearance, these defects can profoundly affect the patient's emotional well-being (Hoeller et al., 2003).

In terms of post-oncologic breast reconstruction options, autologous tissue transfer using vascularized flaps of skin, fat, and muscle remains the current gold standard treatment following mastectomy. Autologous tissue transfer using free flaps leads to a more natural-looking reconstruction with reproducible and increasingly aesthetic results while they pose low complication rates typically less than 2% (Serletti et al., 2011; Ochoa et al., 2012; Teymouri et al., 2006). Furthermore, in case of reconstruction using transverse rectus abdominis musculocutaneous (TRAM) flaps, excessive tissue and fat are extracted from the abdomen area which may be of interest to many women (Serletti et al., 2011). However, some thin women or breast-cancer-patients who require bilateral reconstruction may have insufficient abdominal tissue for this procedure, hence cannot be considered for this cosmetic approach (Roehl et al., 2010; Kronowitz et al., 2003; Kroll, 1998). Synthetic implants are an alternative, but the fibrous encapsulation of these devices following implantation can cause severe pain, implant migration, and rupture (Beahm et al., 2003; Necchi et al., 2011; Bodin et al., 2015; Lim et al., 2013). While approximately 70% of breast cancer patients now opt for lumpectomy (Chatterjee et al., 2015; Agarwal et al., 2014), there are fewer reconstructive options with this more conservative approach. In fact, scarring and asymmetries are often left untreated or addressed through contralateral breast reduction surgery to balance the lost volume.

An alternative clinical strategy is autologous tissue transfer, which involves removing excess adipose tissue from one depot in the body using liposuction procedures and implanting it in the breast. With recent developments in liposuction surgeries significant amounts of excess fat can be detached from different parts of the body using small openings and a suction cannula, and then utilized for augmentation or reconstruction of the breast (Hamza et al., 2013; Kim et al., 2014). The performance of fat grafting reported by plastic surgeons has been good, especially in correcting contour irregularities and deformities in mastectomy patients (ASPRS Ad-Hoc Committee on New Procedures, 1987; Spear et al., 2005). Nonetheless, there are controversial reports concerning safety of the autologous fat grafts for breast tissue reconstruction purposes. One issue is interference of fat graft with subsequent radiologic techniques for diagnosis of potential cancerous parts within the breast. Other issues include probable influence on neoplasia formation arising from unexpected fat reabsorption and possible contribution of the transplanted stem cells to possibly provoke new cancer concurrence (Kim et al., 2014; Gutowski, 2009; Pearl et al., 2012).

An emerging strategy for soft tissue restoration is the design of biomaterial scaffolds which have the ability to maintain the required three-dimensional volume and ideally, would promote the regeneration of the patient's own healthy tissues (Beahm et al., 2003). Various types of synthetic and naturally-derived scaffolds have been explored for this application (Flynn and Woodhouse, 2008). In particular, decellularized adipose tissue (DAT) scaffolds have shown great promise due to their natural ability to support fat formation (Flynn, 2010; Turner et al., 2012; Yu et al., 2013). To generate these types of scaffolds, adipose tissue is subjected to a biochemical decellularization process designed to extract cells and lipid from the tissue in order to reduce potential immunogenicity in allogenic applications, while conserving the structure and composition of the extracellular matrix (ECM) as much as possible (Flynn, 2010; Badylak, 2002). In addition, another new option is hyaluronic acid (HA) biomaterial that has been investigated as an adipose tissue-engineering platform for breast augmentations and enhancements (Flynn et al., 2007, 2009; Heden et al., 2011; Bhat et al., 2011). While HA-based biomaterials such as Macrolane have some benefits such as biocompatibility and consonance with minimally invasive implantation procedure under local anesthesia, there are serious concerns regarding the suitability and applicability of the HA-based materials for breast reconstruction (Goisis, 2012; Goisis et al., 2011). Durability and cost of HA-based materials for breast augmentation applications are major concerns. Available HA-based materials are bio-degradable while ~60% rate of resorption has been reported in 1 year after treatment using these materials (Goisis, 2012; Goisis et al., 2011). Consequently, these biomaterials cannot be used effectively unless multiple retreatments are planned, which maybe cost prohibitive especially since three to four subsequent touch-ups are typically necessary to achieve satisfactory results (Goisis, 2012; Goisis et al., 2011). Furthermore, since the absorption rate varies among patients, more imaging examination procedures including Magnetic Resonance (MR) or ultrasounds imaging are necessary to estimate required retreatment volume,