Materials Science and Engineering C 57 (2015) 338–343

Contents lists available at ScienceDirect

Materials Science and Engineering C

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

The effect of post-mastectomy radiation therapy on breast implants: Unveiling biomaterial alterations with potential implications on capsular contracture

Diego Ribuffo [a], Federico Lo Torto [a], Sara M. Giannitelli [b], Marco Urbini [c,d], Luca Tortora [c,d], Pamela Mozetic [b], Marcella Trombetta [b], Francesco Basoli [e], Silvia Licoccia [e], Vincenzo Tombolini [f,g], Raffaele Cassese [f], Nicolò Scuderi [a], Alberto Rainer [b,h,*]

[a] Department of Plastic Surgery, "Sapienza" University of Rome, Viale del Policlinico 155, 00166 Rome, Italy
[b] Tissue Engineering Unit, Department of Engineering, Università Campus Bio-Medico di Roma, Via Álvaro del Portillo 21, 00128 Rome, Italy
[c] Surface Analysis Laboratory, Department of Mathematics and Physics, University "Roma Tre", Via della Vasca Navale 84, 00146 Rome, Italy
[d] INFN — National Institute of Nuclear Physics, Section of Roma Tre, Via della Vasca Navale 84, 00146 Rome, Italy
[e] Department of Chemical Science and Technologies, University of Rome "Tor Vergata", Via della Ricerca Scientifica 1, 00173 Rome, Italy
[f] Department of Radiation Oncology, "Sapienza" University of Rome, Viale del Policlinico 155, 00166 Rome, Italy
[g] Spencer-Lorillard Foundation, Viale Regina Elena 291, 00161 Rome, Italy
[h] IFN — Institute for Photonics and Nanotechnologies, National Research Council, Via Cineto Romano 42, 00156 Rome, Italy

ARTICLE INFO

Article history:
Received 22 December 2014
Received in revised form 11 May 2015
Accepted 9 July 2015
Available online 18 July 2015

Keywords:
Post-mastectomy radiation therapy (PMRT)
Capsular contracture
Silicone breast implants
Surface analyses

ABSTRACT

Post-mastectomy breast reconstruction with expanders and implants is recognized as an integral part of breast cancer treatment. Its main complication is represented by capsular contracture, which leads to poor expansion, breast deformation, and pain, often requiring additional surgery. In such a scenario, the debate continues as to whether the second stage of breast reconstruction should be performed before or after post-mastectomy radiation therapy, in light of potential alterations induced by irradiation to silicone biomaterial. This work provides a novel, multi-technique approach to unveil the role of radiotherapy in biomaterial alterations, with potential involvement in capsular contracture. Following irradiation, implant shells underwent mechanical, chemical, and microstructural evaluation by means of tensile testing, Attenuated Total Reflectance Fourier Transform InfraRed spectroscopy (ATR/FTIR), Scanning Electron Microscopy (SEM), high resolution stylus profilometry, and Time of Flight Secondary Ion Mass Spectrometry (ToF-SIMS).
Our findings are consistent with radiation-induced modifications of silicone that, although not detectable at the microscale, can be evidenced by more sophisticated nanoscale surface analyses. In light of these results, biomaterial irradiation cannot be ruled out as one of the possible co-factors underlying capsular contracture.

1. Introduction

Breast reconstruction with expanders and implants is one of the most popular reconstruction options after mastectomy, in addition to autologous tissue reconstruction. The advantages of this technique include low surgical invasiveness and good esthetic outcome, without the visible skin color mismatch often seen in free flap transfer [1]. The main complication of implant-based reconstruction is represented by fibroproliferation of the capsular tissue around the breast implant with resultant capsular contracture. This leads to poor expansion and breast distortion with unsatisfactory esthetic outcome and pain, often mandating for additional surgery. At present, the pathogenic mechanism underlying capsular contracture is still unknown [2]. It is certainly a multifactorial process, resulting from human body reaction, biofilm activation, bacteremic seeding, or silicone exposure [3,4].

In such a scenario, the debate continues as to whether the second stage of breast reconstruction should be performed before or after post-mastectomy radiation therapy (PMRT). This has become even more important in light of the increasing use of one-stage implant based reconstruction, with immediate implant placement at the time of mastectomy [5]. Indeed, while the nature of radiation effects on soft tissues has been deeply investigated [6], only few studies have examined radiation effects on breast implants [7]. For this reason, it appears of utmost importance to characterize the behavior of prosthetic materials exposed to radiotherapy protocols, with the aim to gather new insights on radiation-induced material alterations, potentially concurring to capsular contracture.

* Corresponding author at: Department of Engineering, Tissue Engineering Unit, Università "Campus Bio-Medico di Roma", Via Álvaro del Portillo 21, 00128 Rome, Italy.
E-mail address: a.rainer@unicampus.it (A. Rainer).

http://dx.doi.org/10.1016/j.msec.2015.07.015
0928-4931/

Besides conventional mechanical and morphological characterization techniques, research in the field of biomaterials can rely on a panel of analytical methodologies for assessing material characteristics at the molecular scale. Fourier Transform InfraRed spectroscopy (FTIR) represents a well consolidated technique, already successfully applied to the study of silicone breast implants [8]. Additionally, Time of Flight Secondary Ion Mass Spectrometry (ToF-SIMS) is gaining increased popularity to analyze surface properties of organic and biomaterials due to its surface sensitivity, chemical specificity, and imaging capability [9,10].

The present work pursues a multi-technique approach addressing morphological and chemical alterations of silicone breast implants exposed to a clinically relevant irradiation, with the aim to elucidate potential degradation mechanisms that might concur to capsular contracture.

2. Methods

Textured medical grade silicone implants (200 cm^3 Siltex^{TM} round high profile gel breast implant, Cohesive II^{TM}, lot# 5868991) were kindly provided by Mentor (Mentor Medical Systems BV, Leiden, The Netherlands). According to the manufacturer's specifications, the gel-filled shell was constructed of successive cross-linked layers of silicone elastomer. In order to study the effect of radiotherapy on the implants, silicone prostheses were wrapped in a bolus that simulated the characteristics of the surrounding soft tissue and underwent irradiation according to a standardized radiotherapy protocol for the treatment of breast cancer. The protocol consisted of a total radiation dose of 50 Gy, fractioned into 25 treatments over 5 weeks. Treatments took 5–10 min each, and were administered from Monday to Friday with a rest at the weekend. Non-irradiated prostheses of comparable size were used as a control.

2.1. Mechanical characterization

Mechanical properties were measured using a tensile tester (Instron, model 3365, Norwood, MA, USA) equipped with a 500 N f.s. load cell, according to ISO 37:2011 standard [11]. Dog-bone-shaped specimens with a shaft length of 20 mm and a width of 4 mm were obtained from the shell of each breast implant. Thickness values ranging between 650 and 750 μm were measured using a flat tip micrometer. Experiments were performed in triplicate.

In accordance with Yildirimer et al. [12], an extension rate of 100 mm/min was selected, and the uniaxial tensile test was conducted until failure while recording stress and strain values. Elastic modulus was calculated from the initial quasi-linear part of stress–strain curves. Ultimate tensile strength (UTS) and strain at break were also recorded.

2.2. Surface analysis

Samples of ca. 1 cm^2 were randomly collected (by scissors) from the domed area of each implant shell, cleaned by sonication and dried under a nitrogen stream.

Samples were analyzed by Attenuated Total Reflectance Fourier Transform InfraRed spectroscopy (ATR-FTIR). Spectra (32 scans, 2 cm^{-1} resolution) were recorded on a Nicolet 8700 spectrophotometer (Thermo Fisher Scientific, Waltham, MA) equipped with a Golden Gate MK II Single Reflection Diamond ATR system (Specac).

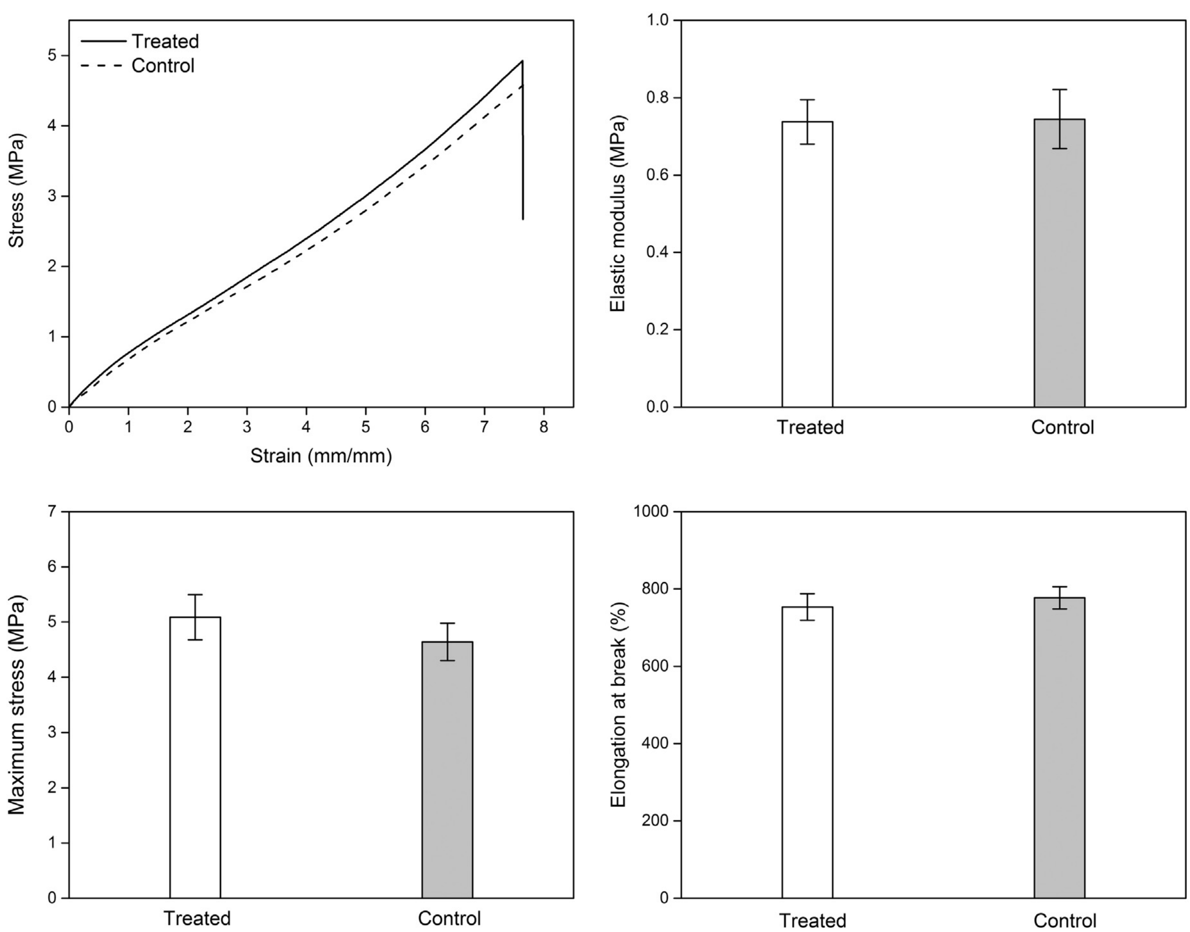

Fig. 1. Top left. Representative stress–strain curves of treated and control specimens. Bar charts of relevant tensile mechanical properties: elastic modulus (top right), ultimate tensile strength (bottom left), and elongation at break (bottom right).