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# Remote controlled non-invasive alternated magnetic field-induced hyperthermia using magnetically functionalized electrospun polyurethane coating for treatment of capsular contracture of synthetic implants

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## Introduction

Implantation of polymeric synthetic biomaterials in human body induces a foreign body reaction and formation of connective tissue capsule around the implants. In case of artificial synthetic breast implantation the accumulation of thick capsular fibrotic tissue and even development of capsular contracture often occurs. It could lead to undesirable cosmetic defects and requires surgical removal of breast implant removal. Similar undesirable outcomes of foreign body reaction in the form of accumulation of thick capsular fibrotic tissue also occurs after implantation of auricular synthetic prostheses used for treatment microtia – a congenital defect in the form of external ear's auricular malformation. For both cases there are no any clinically effective non-invasive therapeutic modalities.

## Electrospinning technology

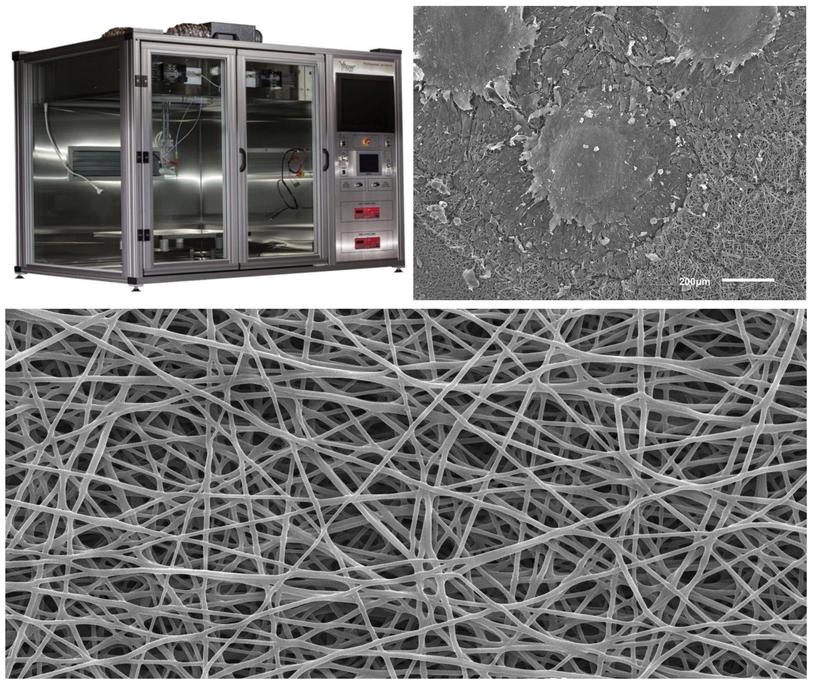


Figure 2.
a) Commercial electrospinning device (Yflow, Malaga, Spain http://www.yflow.com);
b) Scanning electron microscope of tissue spheroids biofabricated from human fibroblasts spreaded on surface of electrospun polyurethane matrices;
c) Scanning electron microscopy of electrospun polyurethane matrix.

## Scheme of coating of implant with magnetically modified electrospun matrix

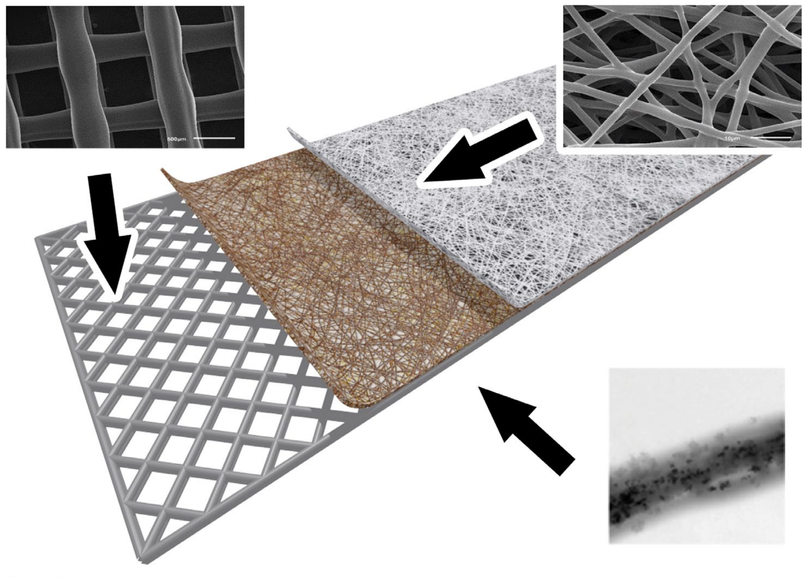

Figure 3.
a) Scanning electron microsopy of polymeric implant fabricated by fused deposition modeling (FDM);
b) Scanning electron microscopy of electrospun polyurethane matrix;
c) Scheme of electrospun double layered coating;
d) Transmission electron microscopy of electrospun fiber containing magnetic iron oxide nanoparticles.

## Capsular contraction

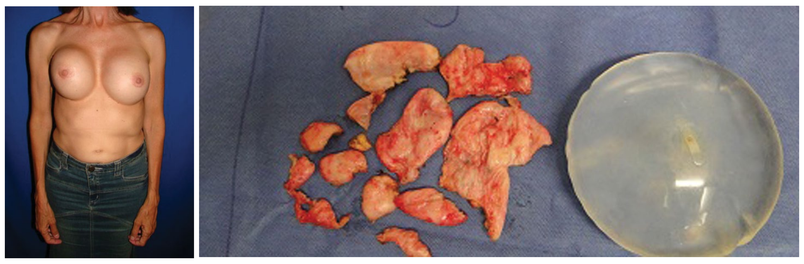

Figure 1.
a) Patient with distorted and displaced breast implant on the right side as a direct result of capsular contracture development;
b) The thick fibrotic tissue from patient with capsular contraction after breast implant removal.

## Magnetically functionalized electrospun matrix

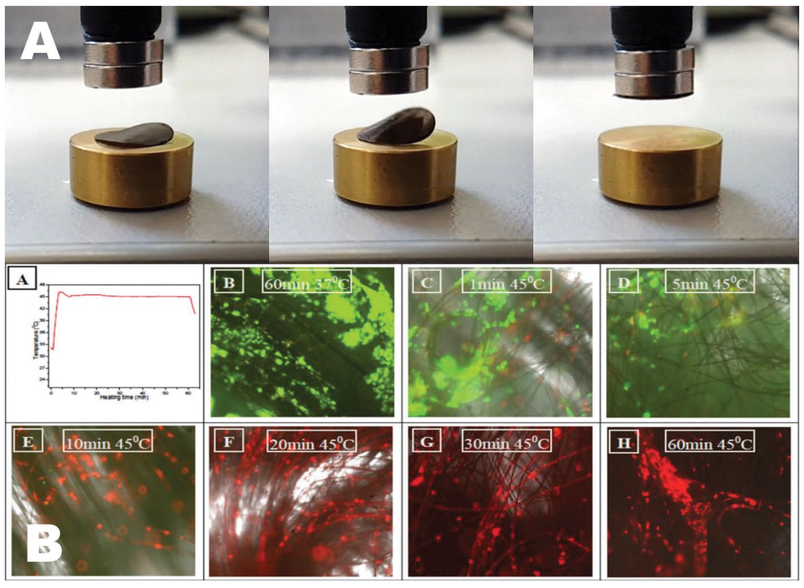


Figure 4.
a) Magnetic levitation of magnetically functionalized of electrospun polyurethane matrix containing magnetic iron oxide nanoparticles;
b) Alternated magnetic field-induced hyperthermia (left side) during 10 minutes at 45 C kills practically all attached cancer cells (green - living cells, red - death cells) (according to Huang C et al. Adv. Funct. Mater. 2012 Ref. 3).

## Thermovision of alternated magnetic field induced hyperthermia

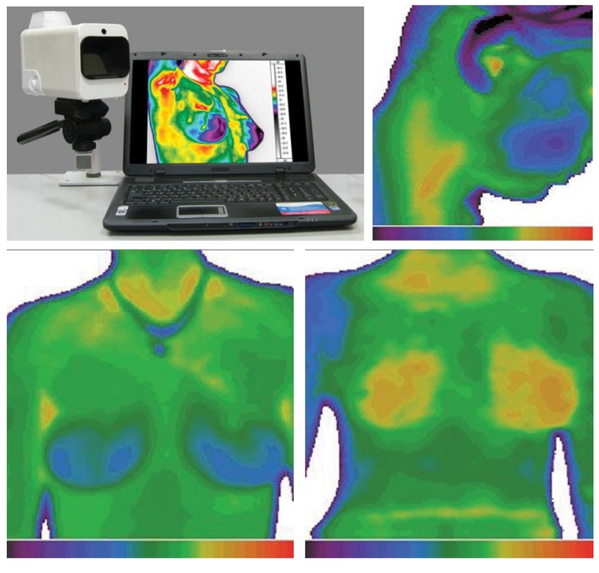

Figure 6.
a) Commercial medical thermovision camera (Russia); b) Thermovision of human ear (violet); c) Thermovision of normal women breast (blue); d) Thermovision of women breast during menstruation (orange).

## Alternated magnetic field generator

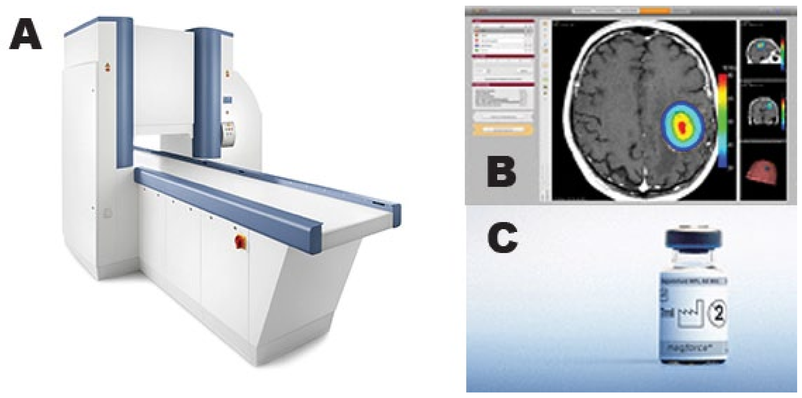


Figure 5.
a) Commercial alternated magnetic field generator (according to MagForce AG, Germany, http://www.magforce.de/en/home.html);
b) Computer visualization of treated by magnetic induced hyperthermia brain glioblastoma tumor (according to (MagForce AG, Germany, http://www.magforce.de/en/home.html);
c) Commercial magnetic iron oxide nanoparticles (according to (MagForce AG, Germany, http://www.magforce.de/en/home.html).

## Results

Auricular implants have been fabricated using fused deposition modeling from non-biodegradable and biocompatible polyurethane. Magnetically functionalized electrospun polyurethane matrices have been fabricated using commercial electrospinning device (Yflow, Spain) and custom made iron oxide nanoparticles. The magnetic nanoparticles size redistribution and their density in magnetically functionalized electrospun polyurethane matrices have been estimated using transmission electron microscopy. Magnetization of magnetically functionalized electrospun polyurethane matrices has been confirmed by using magnetometer and magnetic levitation. The desirable level of hyperthermia (up to 45 C) has been achieved in vitro by using alternated magnetic field generator. Mathematical modelling using finite element analysis (FEA) predicted certain improvement of material properties of synthetic auricular implants coated with electrospun polyurethane matrices. Testing of material properties of printed auricular polyurethane implants coated with electrospun matrices using three point flexure method indeed demonstrated increasing rigidity of hybrid synthetic implants. The direct physical interactions between synthetic auricular implant fabricated by fused deposition modeling and nano- and microfibers of electrospun polyurethane coating have been shown using scanning electron microcopy and scanning probe nanotomography. Tissue spheroids biofabricated from human fibroblasts using non-adhesive substrates have been emploied as a test system for estimation of in vitro biocompatibility of electrospun polyurethane matrices. It have been shown that tissue spheroids biofabricated from human fibroblasts attach and spread on the surface of electrospun polyurethane. However, at hyperthermia (45 C) all cells forming tissue spheroids undergo cell death as it have been demonstrated by cytotoxic studies.

## Discussion

Alternated magnetic field-induced hyperthermia using alternated magnetic field generators and intravenously injected magnetic nanoparticles have been successfully tested on experimental animals and proposed for treatment of cancer patients [1]. Recently it have been proposed to use magnetic nanoparticles for magnetic functionalization of electrospun polymeric matrices [2]. Moreover, it have been shown that alternated magnetic field-induced hyperthermia kills all adjacently located tumor cells at temperature 45 C [3-4]. We hypothesize that alternated magnetic field-induced hyperthermia could be also used for treatment of capsular contracture which represents undesirable outcome of foreign body reaction after implantation of synthetic implants such as breast and auricular prostheses.

## Conclusion

Coating of synthetic implants with very thin layer of magnetically functionalized with magnetic nanoparticles electrospun polymer matrix enable repeating cycles of hyperthermia using remotely controlled alternated magnetic field generators and create novel therapeutic modality for treatment of capsular contracture. It will guarantee targeted remote controlled non-invasive ablation of undesirable thick capsular fibrotic tissue in cases with capsular contracture without need for surgical removal and replacement of synthetic implants. In vivo animal studies of auricular implants coated with magnetically functionalized electrospun matrices is a next logical step in the development of this promising technology.

## Acknowledgements

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## References

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