Rapid prototyped nano composite magnetic scaffolds for osteochondral tissue regeneration

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Additive Manufacturing
  - opportunities in Tissue Repair & Regeneration

Nano-composite magnetic scaffolds
  - Iron Oxide & Iron doped Hydroxyapatite (MNPs)
  - PCL/MNPs PEG/MNPs nanocomposites
  - Properties of superparamagnetic scaffolds

Features of superparamagnetic scaffolds used in conjunction with
magnetically labeled cells

RP of nanocomposite scaffolds for osteochondral tissue regeneration
Additive Manufacturing opportunities in the MedTech industry (non-implantable devices)

Indirect Application of AM (molding)

Direct Application of AM

Ink-jet

STL

FDM

Spraybase
Additive Manufacturing opportunities in the MedTech industry (implantable devices)

MSC-loaded collagen-LMW HA-4S-StarPEG sIPN

3D Bioplotting in conjunction with solvent casting/phase inversion

Combination of 3D Photo-Printing and 3D Fiber Deposition techniques

Combination of 3D Fiber Deposition Technique and Electrospinning
Rationale for manufacturing magnetic scaffolds

on demand drug delivery

MNP

Bioaggregate

MNP

Cell

Magnetic Scaffold

smart cell seeding

Magnet
Iron Oxide & Iron Doped Hydroxyapatite MNPs

Superparamagnetic nanoparticles

Fe₃O₄@PAA

Fe²⁺/Fe³⁺

FeHA

Ca₅(PO₄)₂·OH
PCL/MNPs & PEG/MNPs nanocomposites

Poly(ε-caprolactone) (PCL)

Stirring & Sonication
PCL/MNPs & PEG/MNPs solutions

Moulding & Solvent Casting
Teflon Mould

Poly(ethylene glycol) diacrylate (PEGDA)
Lucirin-TPO photoinitiator

PCL/MNPs
90/10 to 50/50 w/w

2D nanocomposites pellets

3D Fiber Deposition

Stereolithography
PCL/MNPs nanocomposites

PCL/FeHa 80/20

[Images and spectra showing the distribution of elements such as P, Ca, and Fe]
PCL/MNPs imaging

fiber

μ-CT

Fe₃O₄ filtering

Optical Microscopy

3D scaffold
Effects of MNPs amount

Small-Punch Test (ASTM 2183)
Effects of MNPs amount

Static Magnetic Field

Dynamic Magnetic Field
On demand drug delivery opportunities

Static Magnetic Field

**M (emu/g)**

- 10 layers
- LP_A
- LP_B
- SP_A
- SP_B
- D=4A
- D=4B

**H (T)**

PCL/Fe$_3$O$_4$

80 / 20

Dynamic Magnetic Field

Thermo-responsive dendrimers

- Bound VEGF
- Released VEGF

Core Shell MNP

PAA@MNP

BSD functionalisation

Molecular Collapsing

42°C

**ΔT (°C)**

- small pores 10 layers; m=70 (mg)
- large pores; m=57.3 (mg)
- small pores; m=47.2 (mg)
- 2 specimens; m=41.9 (mg)

**t (s)**

PCL-Fe$_3$O$_4$ 80/20

Magnetic force
PCL/MNPs customized scaffolds for cell assay
PCL/MNPs nanocomposites: in vitro assay

**hMSCs**

- **PCL**
- **PCL/MNPs 90/10**
- **PCL/MNPs 80/20**
- **PCL/MNPs 70/30**

### ALP Activity (ng ALP/ng DNA) vs. Time (days)

- **7 days**
- **14 days**
- **21 days**

PCL/MNPs nanocomposites: contact angle

<table>
<thead>
<tr>
<th>Materials</th>
<th>Contact Angle, θ (deg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCL</td>
<td>81.4 ± 4.4</td>
</tr>
<tr>
<td>PCL/MNPs 90/10</td>
<td>75.7 ± 4.6</td>
</tr>
<tr>
<td>PCL/MNPs 80/20</td>
<td>74.8 ± 2.6</td>
</tr>
<tr>
<td>PCL/MNPs 70/30</td>
<td>64.9 ± 8.2</td>
</tr>
</tbody>
</table>

MNPs provide a nanostructured topography & increase PCL hydrophilicity

TEM Imaging

Russo T, et al. Procedia Eng 2013
Cell growth was 2.2-fold greater than that without the application of a magnetic field.

hMSC loading was 36% higher than seeding without a magnetic field.
Effect of a static magnetic field

V. Goronov et al, submitted to Journal of Tissue Engineering 2017
Effect of a dynamic magnetic field

Sinusoidal magnetic field
f = 70Hz
A = 25-30 mT

Stimulation cycle
18 min. + 54 min. relax

Daily stimulation
6 h/day

hMSC

T Russo et al, Bioactive Materials 2017
PCL/MNPs scaffolds: in vivo behaviour

*In vivo* behaviour of magnetic scaffolds implanted into rabbit femur

Hystological investigation at 4 weeks post-implantation showed mineralized tissue regeneration around and into the scaffold
Scaffolds for osteochondral tissue regeneration

Rational for combining FDM & Stereolithography

Stereolithography
Advantage: stratification thickness
Drawback: amount of inorganic particles

FDM
Advantage: amount of inorganic particles
Drawback: stratification thickness
Scaffolds for osteochondral tissue regeneration
Acknowledgements

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