

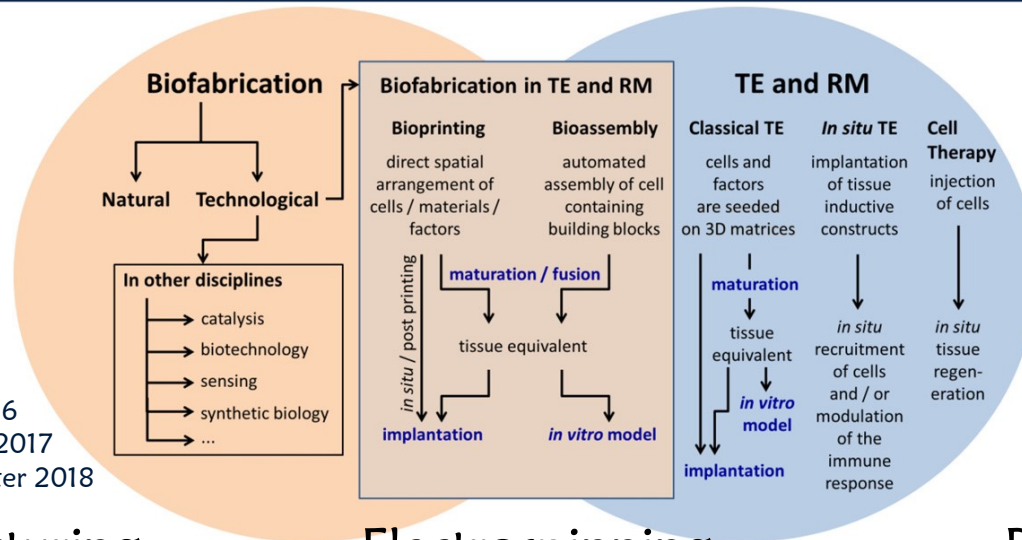


Biostampa a Ultra Alta Fedeltà di tessuti biologici usando lo Spazio per la scoperta di soluzioni anti-invecchiamento con risvolti anche sulla Terra

LORENZO MORONI

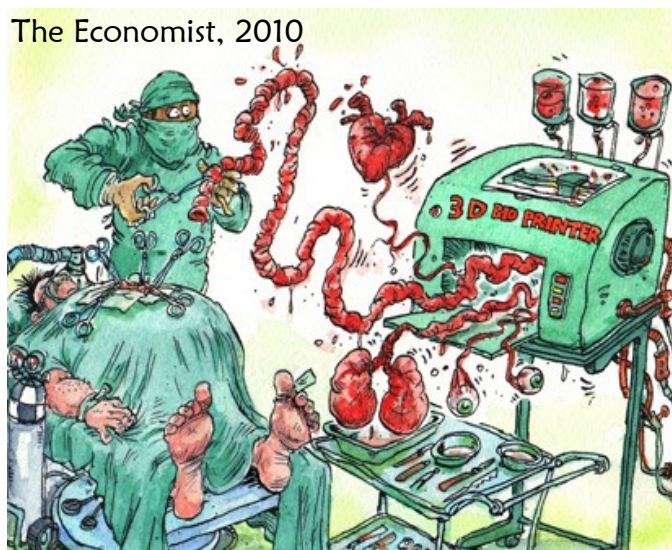
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l.moroni@maastrichtuniversity.nl



Groll J et al., Biofabrication 2016
 Moroni L et al. Trends Biotech 2017
 Moroni L et al. Nature Rev Mater 2018

Additive Manufacturing



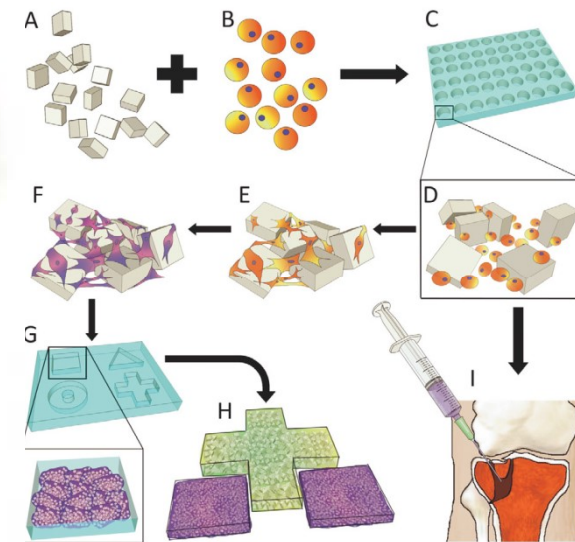
Moroni L et al., J Biomed Mater Res 2005
 Giordano RA, et al., J Biom Sci Polym Edn, 9; 1996

Electrospinning



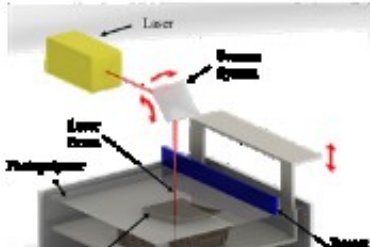
Moroni L et al., Biomaterials 2006
 Li WJ et al., J Biomed Mater Res 2002

Bottom-up

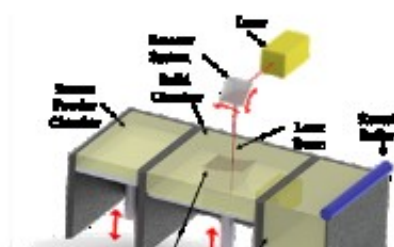


Leferink AM et al., Adv. Materials 2014

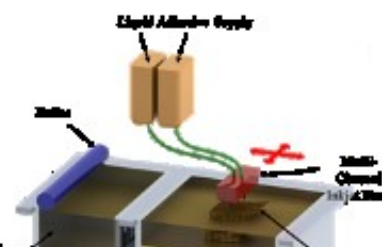
a) Stereolithography (SLA)



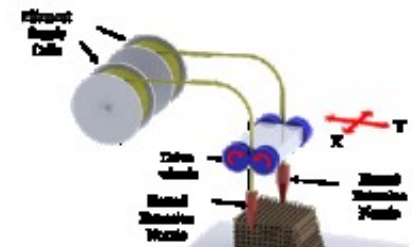
b) Selective Laser Sintering (SLS)



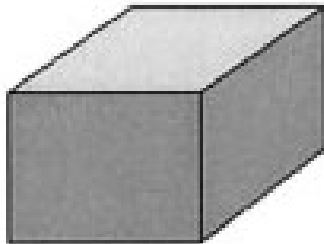
c) Three Dimensional Printing (3DP)



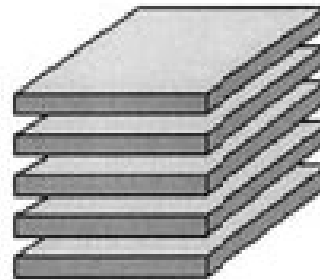
d) Fused Deposition Modelling (FDM)



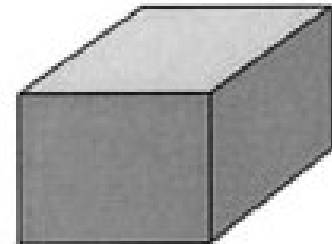
CAD



RP
soft-
ware

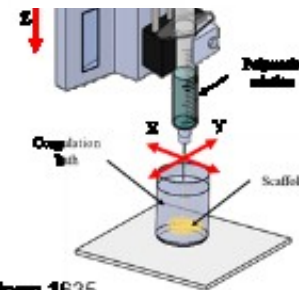
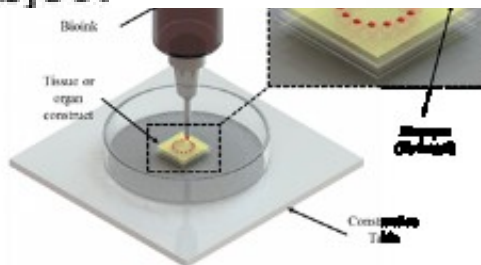
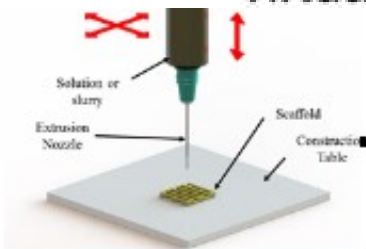


RP

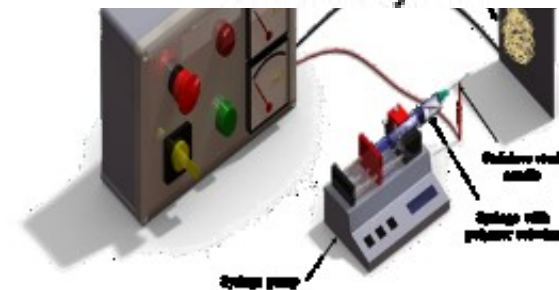


virtual object

real object



Mohs et al, 2012, DOI: 10.1002/jbm.b.1635



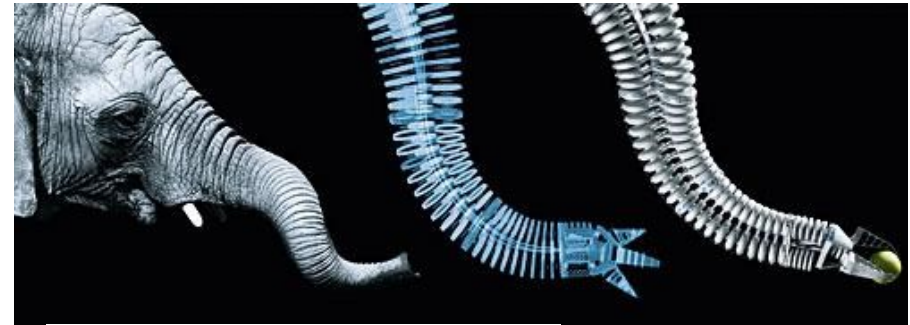
Moroni L et al., J Biomed Mater 2005

Pfister A, et al. J Polym Sci, 42; 2004

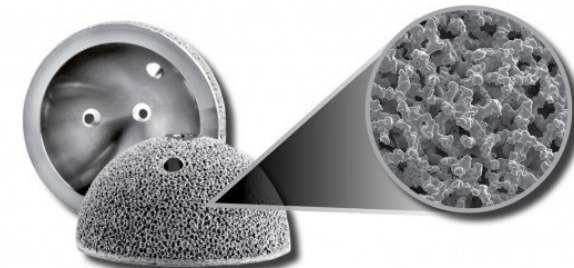
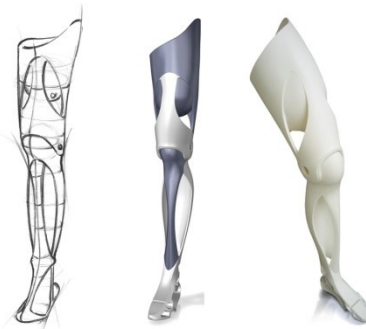
Sun W, et al., Comp Meth Prog Biomed 2002

Additive Manufacturing in the Biomedical World

- Supporting Tools (e.g. exoskeletons)
- Instrumentation
- Dental (e.g. crowns & Bridges; > 10.000 produced daily)
- Ear Implants
- Prostheses
- Visualization supporting tools
- Implants

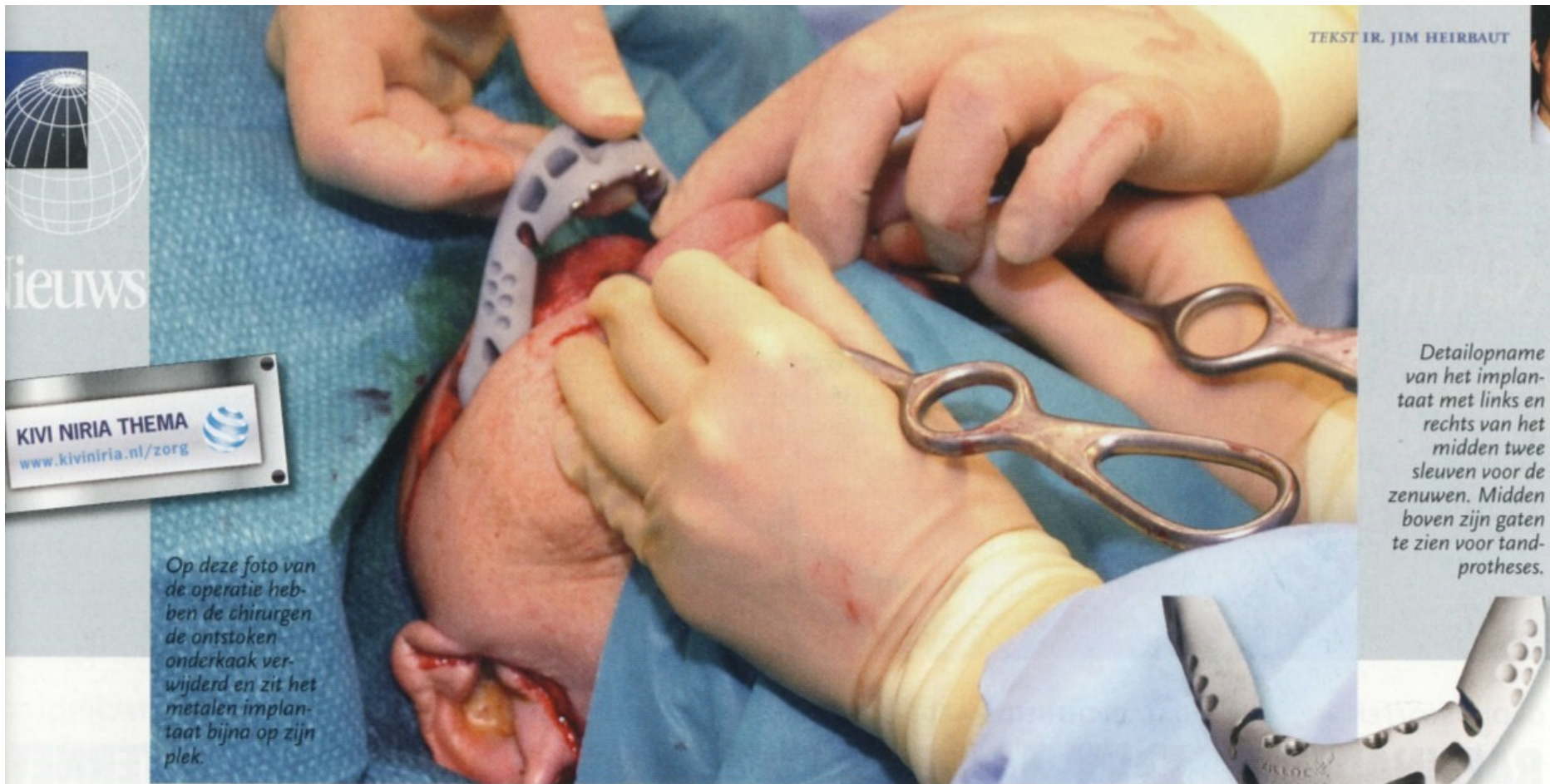


Hettich
ZENTRIFUGEN



**ACETABULAR CUPS: > 40.000
PRODUCED WITH EBM WHERE ~
50% ARE IMPLANTED IN PATIENTS**

First AM Customized Mandible Implanted in a Patient



TEKST IR. JIM HEIRBAUT

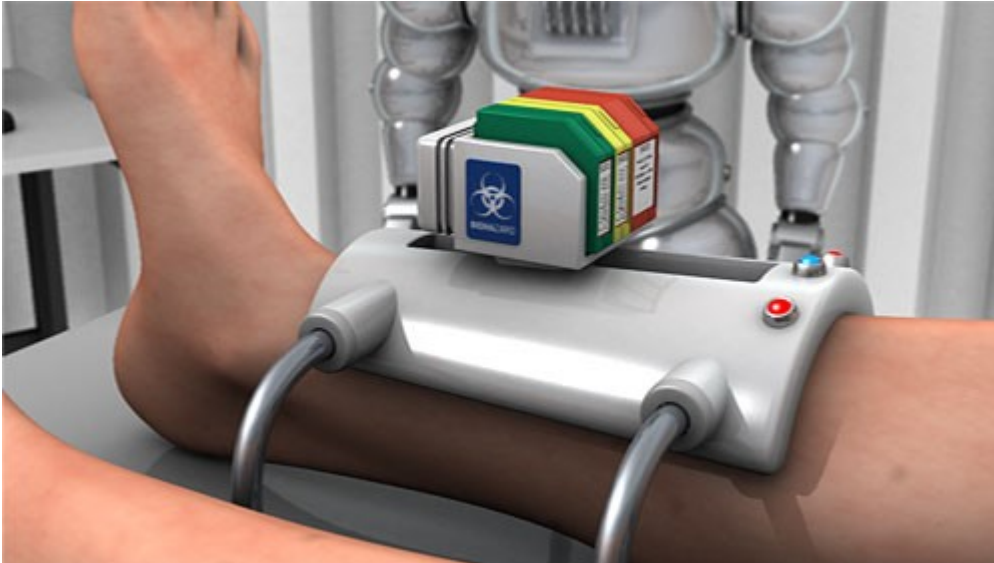
Detailopname van het implantaat met links en rechts van het midden twee sleuven voor de zenuwen. Midden boven zijn gaten te zien voor tandprotheses.

Op deze foto van de operatie hebben de chirurgen de ontstoken onderkaak verwijderd en zit het metalen implantaat bijna op zijn plek.

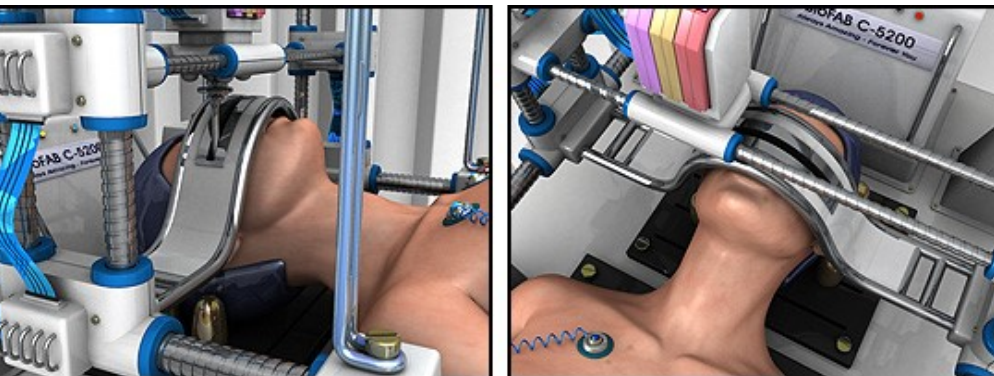
METALEN IMPLANTAAT OPGEBOUWD UIT DUIZENDEN LAAGJES

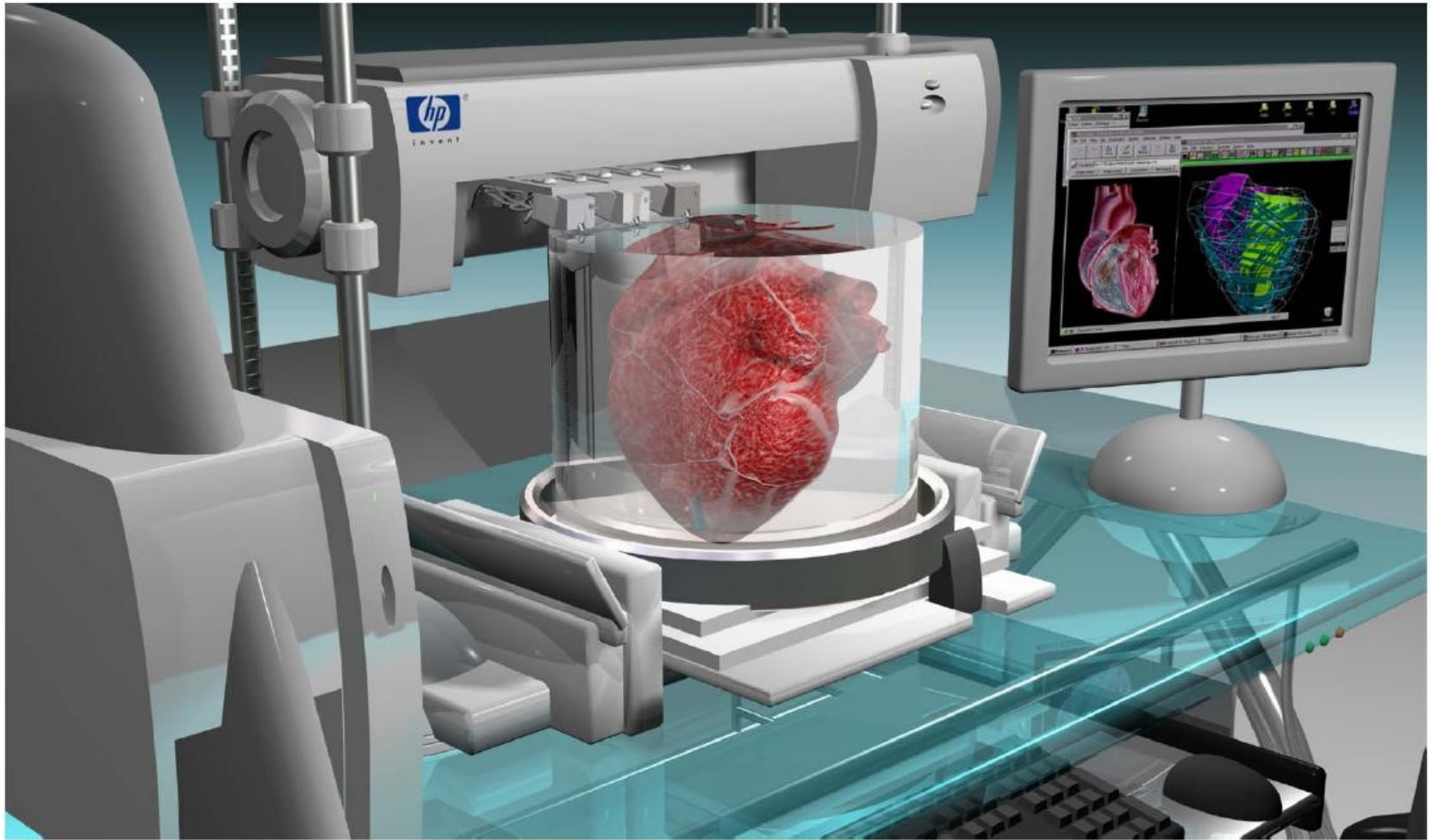
ONDERKAAK IN 3D GEPRINT

Additive Manufacturing in the Biomedical World

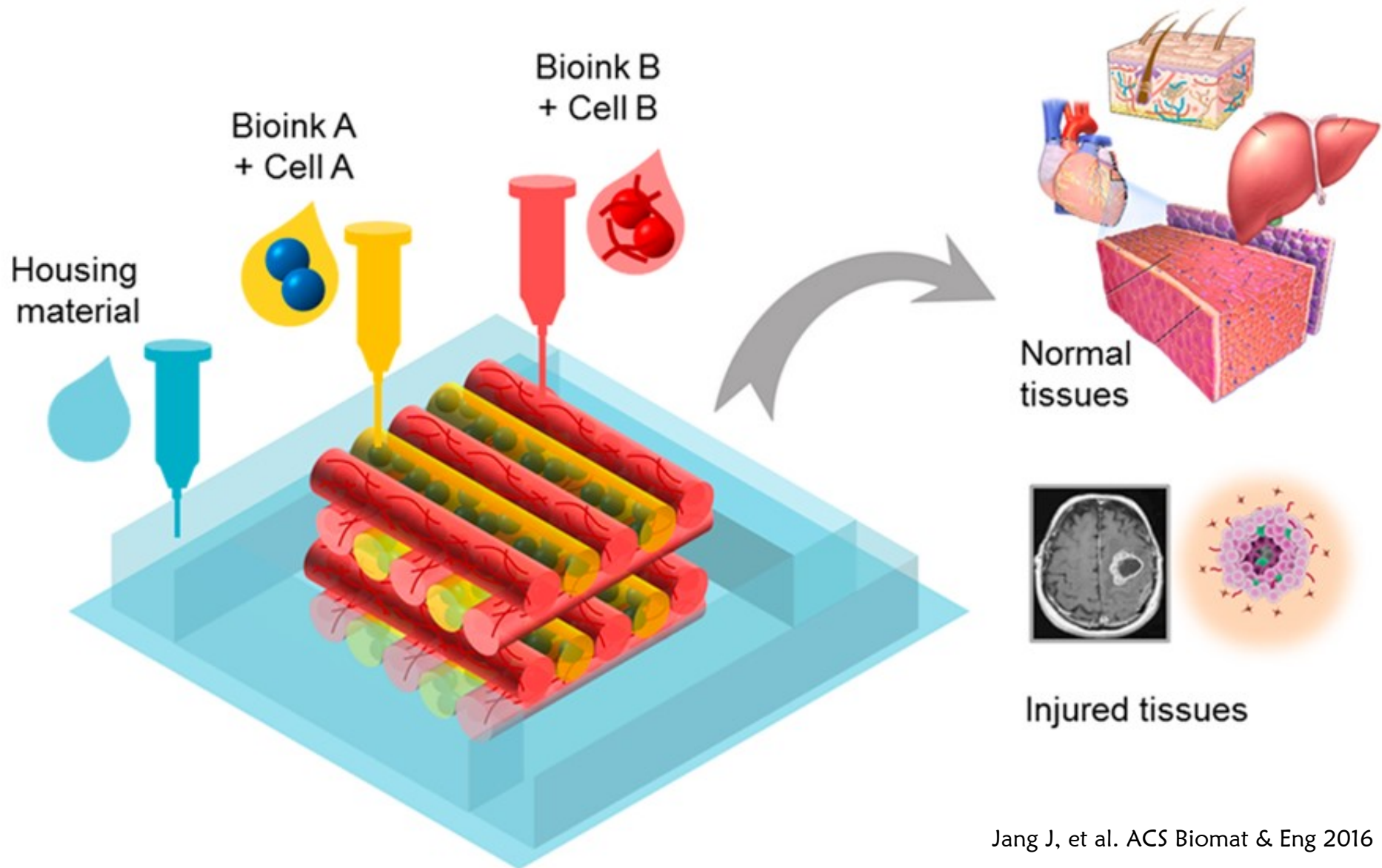


Yoo J., et al. Wake Forest University





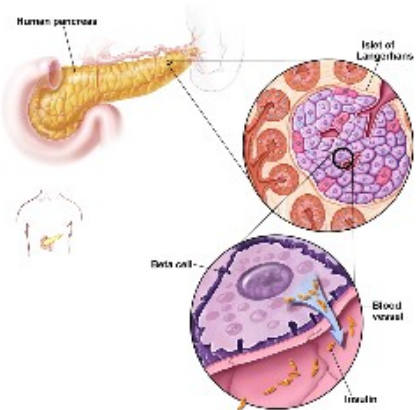
The Future of Biofabrication – in vitro models



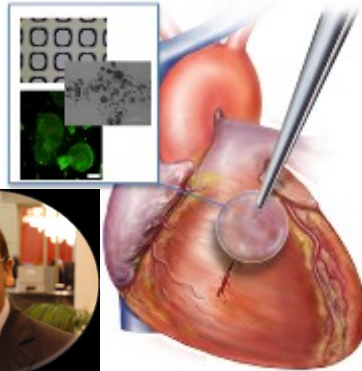
Jang J, et al. ACS Biomater Eng 2016

Towards mimicking biological complexity

Islets transplant



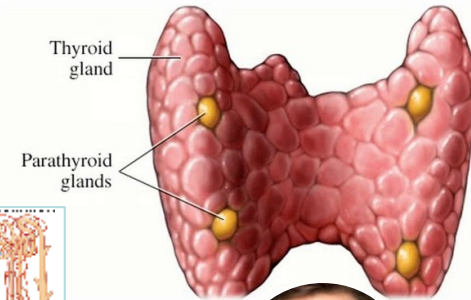
Cardiac tissue model



In vitro nephron

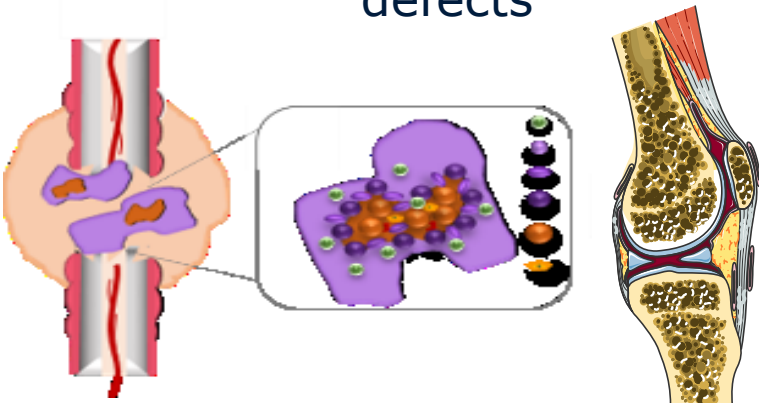


Thyroid 3D Screening

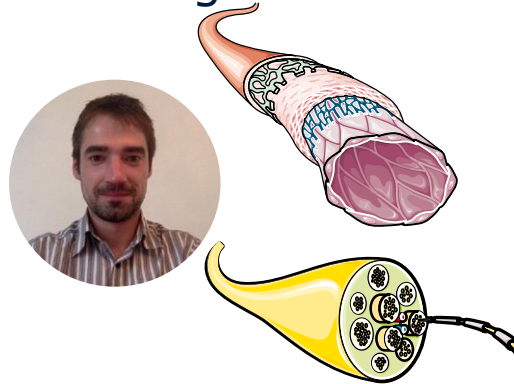


Marchioli G et al., Biofabrication 2015
 Marchioli G et al. Adv Healthcare Mater 2016

Long bone & Osteochondral defects

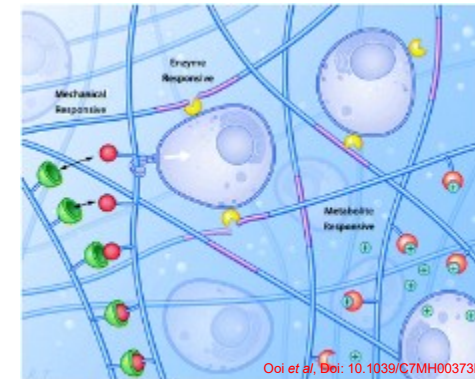


Vascular & Neural regeneration

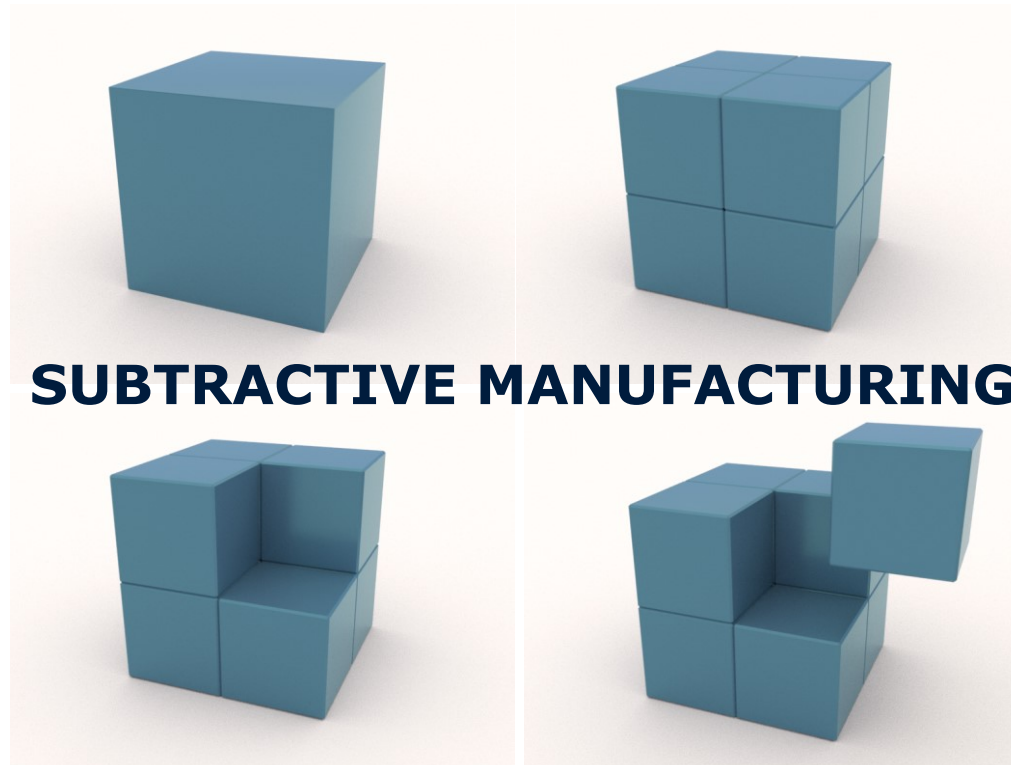


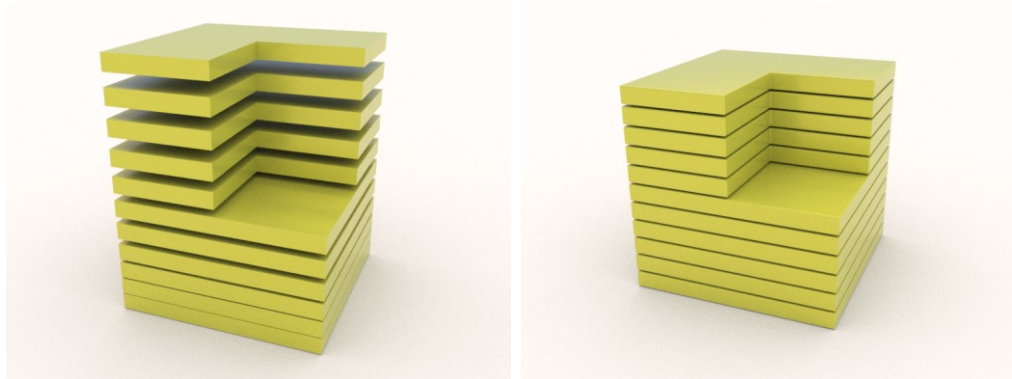
Adapted from: karplab.net
 PMHT0024499
 medinart.eu

New hydrogels

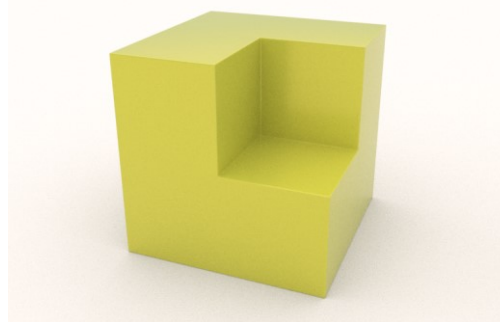


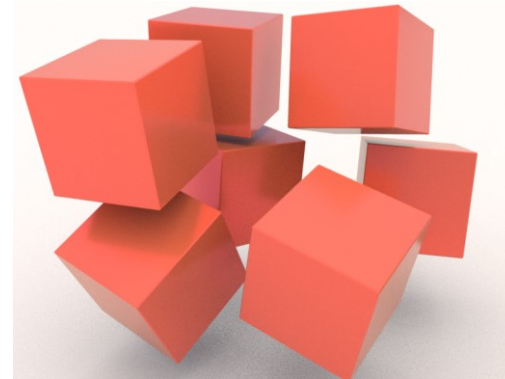
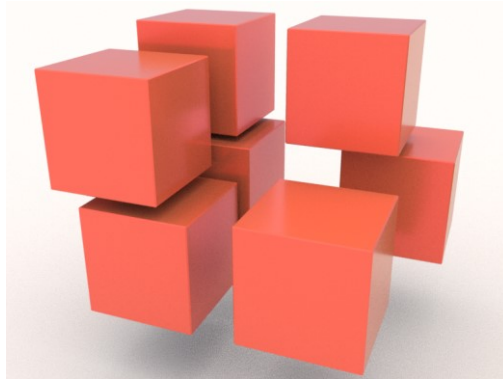
Ooi HW, et al. Biomacromol 2018
 Hafeez S, et al. Gels 2018



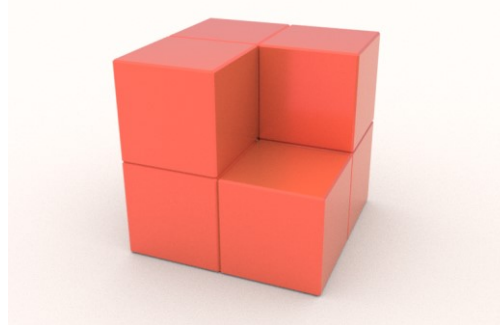


ADDITIVE MANUFACTURING



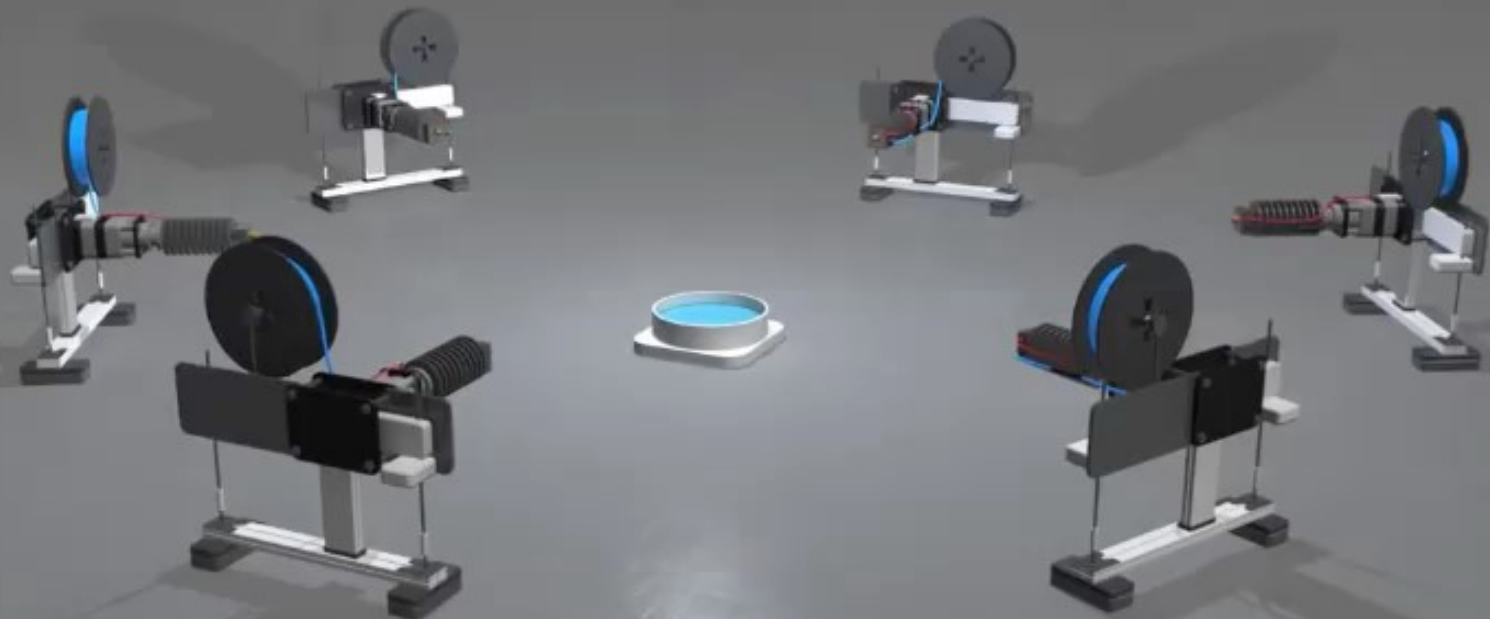


FORMATIVE MANUFACTURING



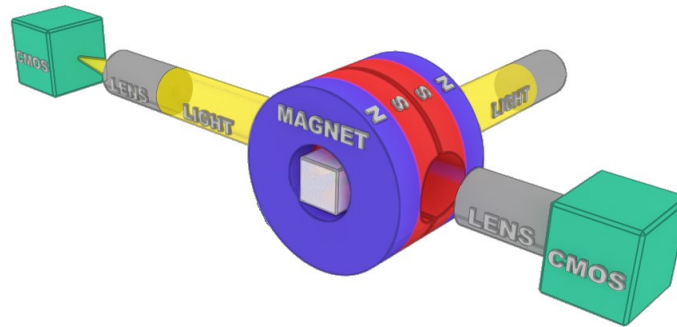
MULTIPLE 3D PRINTERS ARE USED

PatentYogi

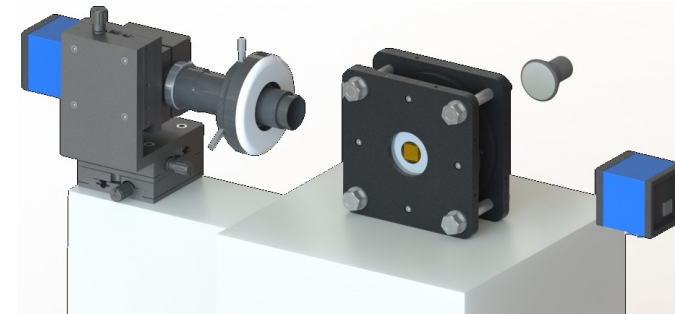




Courtesy
Dr. Vladimir Mironov



Schematic diagram



Experimental setup

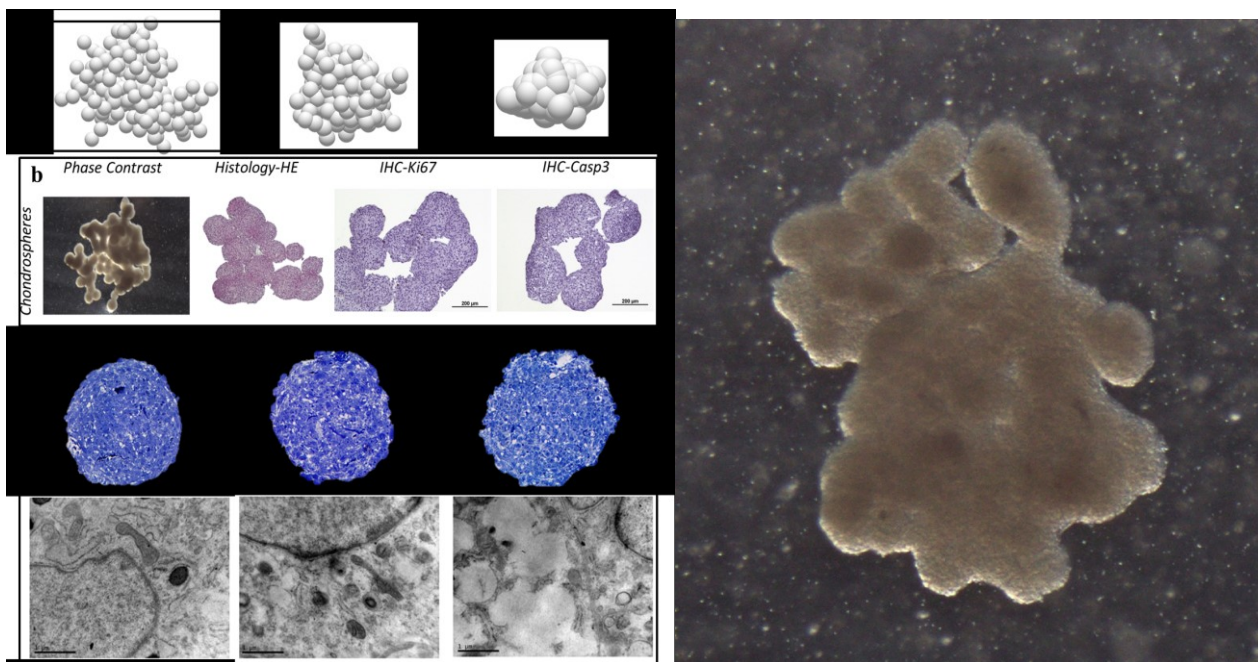
Experimental setup, containing:

- Two annular neodymium magnets, oriented with the same poles to each other;
- glass cuvette with a suspension of paramagnetic and spheroids placed in the axial hole of the magnets;
- backlight;
- video camera



3D model prototype

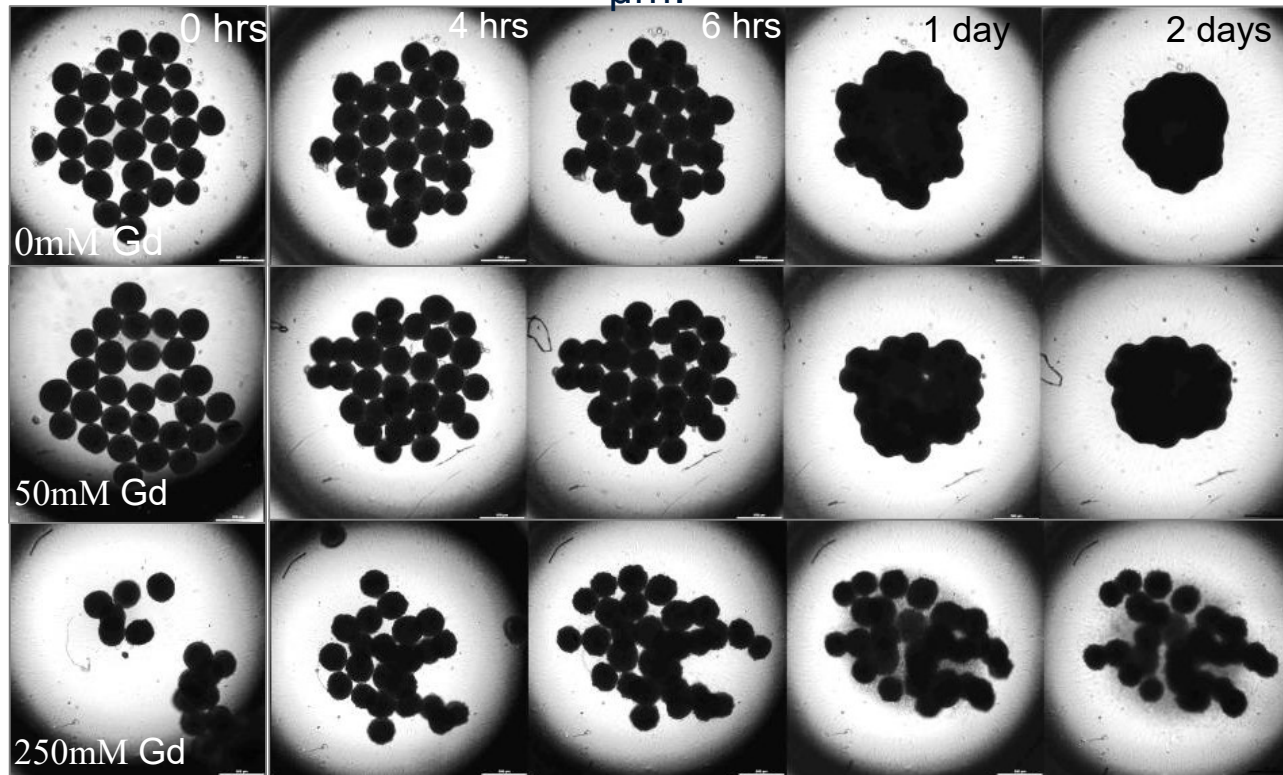
Bioassembly of chondrospheres at ISS and estimation toxicity of paramagnetic salt of gadolinium



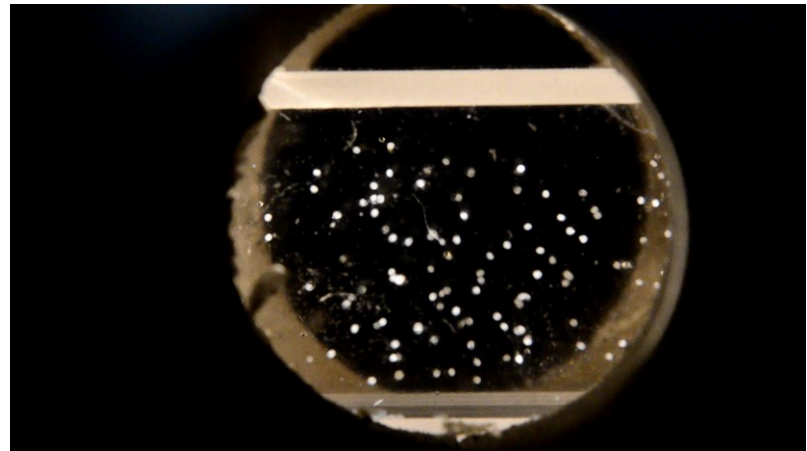
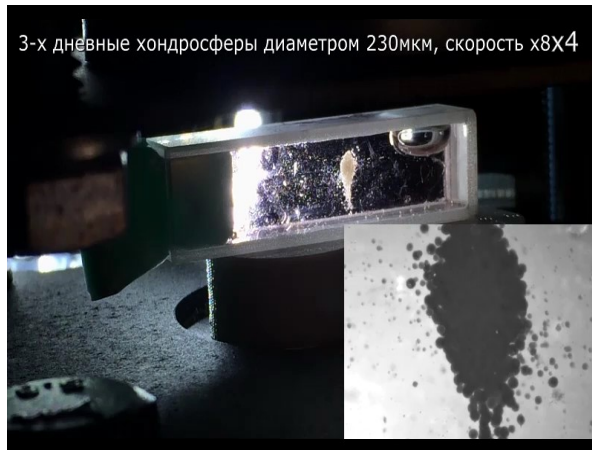
Courtesy
Dr. Vladimir Mironov

Fusion of tissue spheroids as a function of time

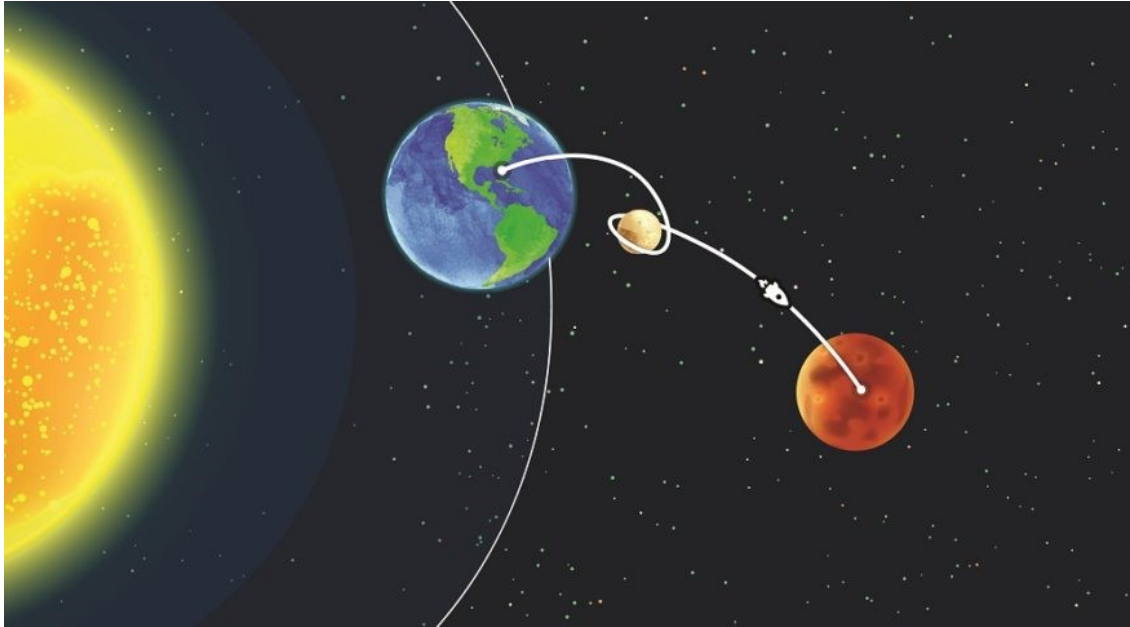
Effect of Gd^{3+} salt on the fusion of 30 tissue spheroids placed in non-adhesive microplate. Phase-contrast images. Scale bar – 500 μm .



Scaffold-Free, Label-Free & Nozzle-Free Magnetic Levitational Assembly of Tissue Engineered Construct from Tissue Spheroids (Chondrospheres)



3D Printing of Living tissues for Space Exploration



1. To develop new bioprinting technology based on magneto-acoustic principles that can be used to rapidly fabricate 3D *in vitro* models that better mimic our organ architecture making advantageous use of μg in space;
 - a. Use of μg will enable a better understanding of levitation principles and physical phenomena at the base of object clustering (cells in our case), which could be reverted back to design criteria for magneto-acoustic bioprinting.
2. To study the effect of radiation and μg on the bioprinted 3D *in vitro* models; as a case study, we propose a heart 3D *in vitro* model.
 - a. 3D *in vitro* bioprinted models could offer a more biologically relevant platform (duration of experiments and reliability of readouts) compared to other available 2D and 3D cell culture models engineered on ESA ground-based facilities.
3. To exploit space conditions as an accelerator of ageing and exposure to environmental chronic conditions on Earth.
 - a. 3D *in vitro* bioprinted models in space could be used to study ageing and exposure to environmental chronic conditions on Earth, providing a viable technology for long-term manned missions to the Moon and Mars.

- **For Human Space Activities:**

- 3D Models to study treatments for:
 - microgravity related diseases (e.g. osteoporosity, muscle loss);
 - Radiation related diseases (e.g. glands and reproductive system);
 - ...

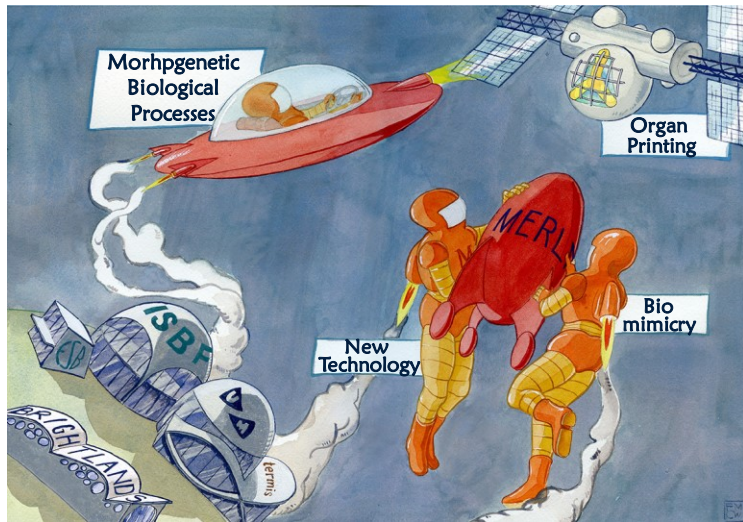
- **Organ Shortage:**

- 1) Kidney;
- 2) Liver;
- 3) Pancreas;
- 4) Heart;
- 5) ...

- **For Global Health:**

- 1) 3D models for pandemic diseases;





- 1) In Roadmap 2 - SOFT OR COMPLEX MATTER RESEARCH IN SPACE, we will contribute to the physics of emulsions, granular matter, colloidal systems, and macromolecules, considering the composition of a bioprinted biological construct has components associated to all these physical forms of matter.
- 2) In Roadmap 6 – UNDERSTANDING THE IMPACT OF GRAVITY ON BIOLOGICAL PROCESSES, CELLS AND ORGANISMS, we contribute to questions A (How are Cell Structure and Function Influenced by the Influence of Gravity?) and B (How Do Gravity Alterations Affect Animal and Human Systems at a Cellular/Tissue Level), at a cellular and tissue/organ level.
- 3) In Roadmap 7 - SUPPORTING LIFE IN HOSTILE ENVIRONMENTS, we contribute in relation to long manned missions in space (e.g. first mission to Mars, or Moon village).
- 4) In Roadmap 8 - UNDERSTANDING AND PREVENTING PHYSIOLOGICAL ADAPTATIONS TO REDUCED GRAVITY, we contribute in terms of really understanding with these human models how certain functionalities will be influenced and how these models could be used to study possible countermeasures.

Technology Development

Biological Assessment



Hardware & Logistics
for Space Missions

Management & Dissemination



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