

Brza izrada prototipova i alata

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Dalji razvoj AM tehnologija

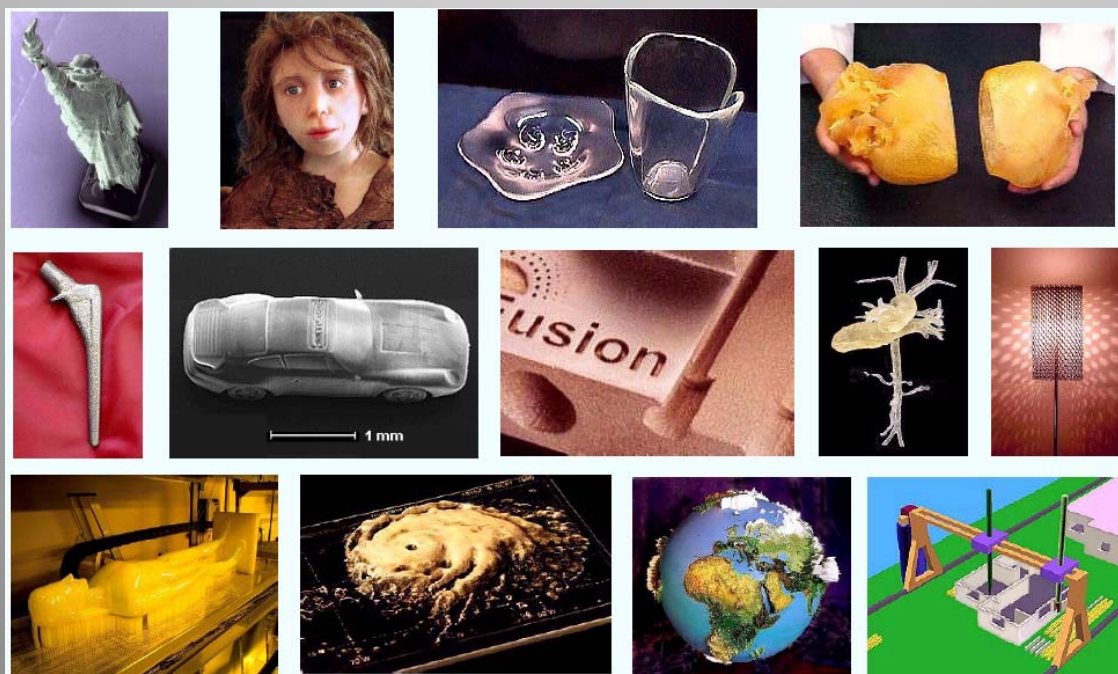
PRINTING THE FUTURE

Tehničke karakteristike:

- a) povećanje brzine izrade modela
- b) povećanje tačnosti modela
- c) novi materijali za AMmodele
- d) povećanje dimenzija modela
- e) telegenerisanje proizvoda na zahtev

Oblasti:

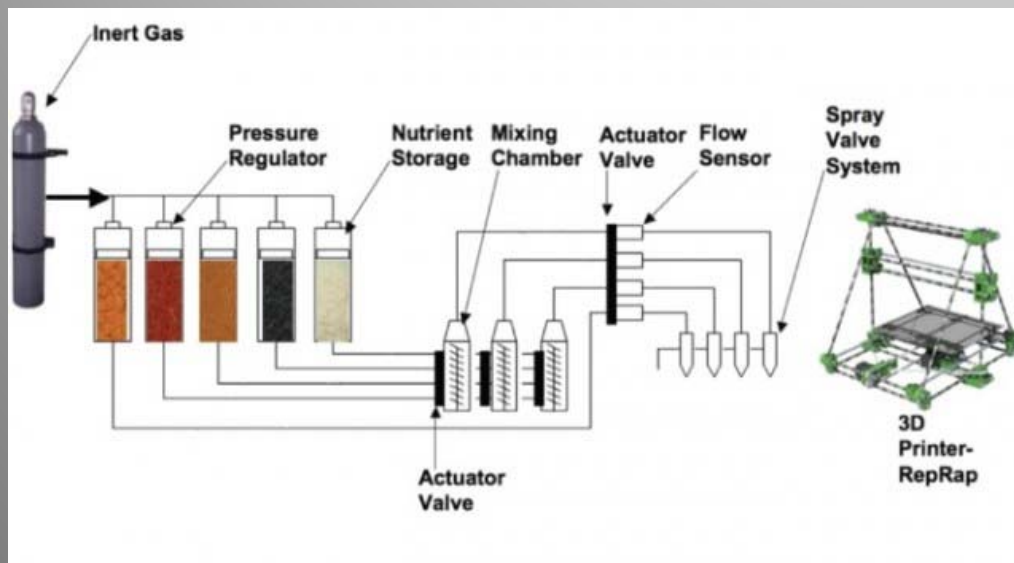
- a) **Medicina - 3D bioprinting**
- b) Proizvodnja hrane
- c) Građevina
- d) 3D za kućnu primenu
- e) Avio-industrija



3D Printing Aims to Deliver Organs on Demand (3D štampa organa na zahtevo)



NASA awarded a \$125,000 grant to develop a process for 3D printing food for astronauts (3D štampači za pripravljanje hrane astronauta)



NASA Funds 3D-Bio-Printer Development to Combat Universal Hunger

ADDITIVE MANUFACTURING & 3D PRINTING

Revolutionizing Breast Cancer Prevention With 3D Printing

ADDITIVE MANUFACTURING & 3D PRINTING

Digital Manufacturing Accelerates Medical Device Innovation

ADDITIVE MANUFACTURING & 3D PRINTING

Additive Manufacturing Aids Surgery at Mayo Clinic

ADDITIVE MANUFACTURING & 3D PRINTING

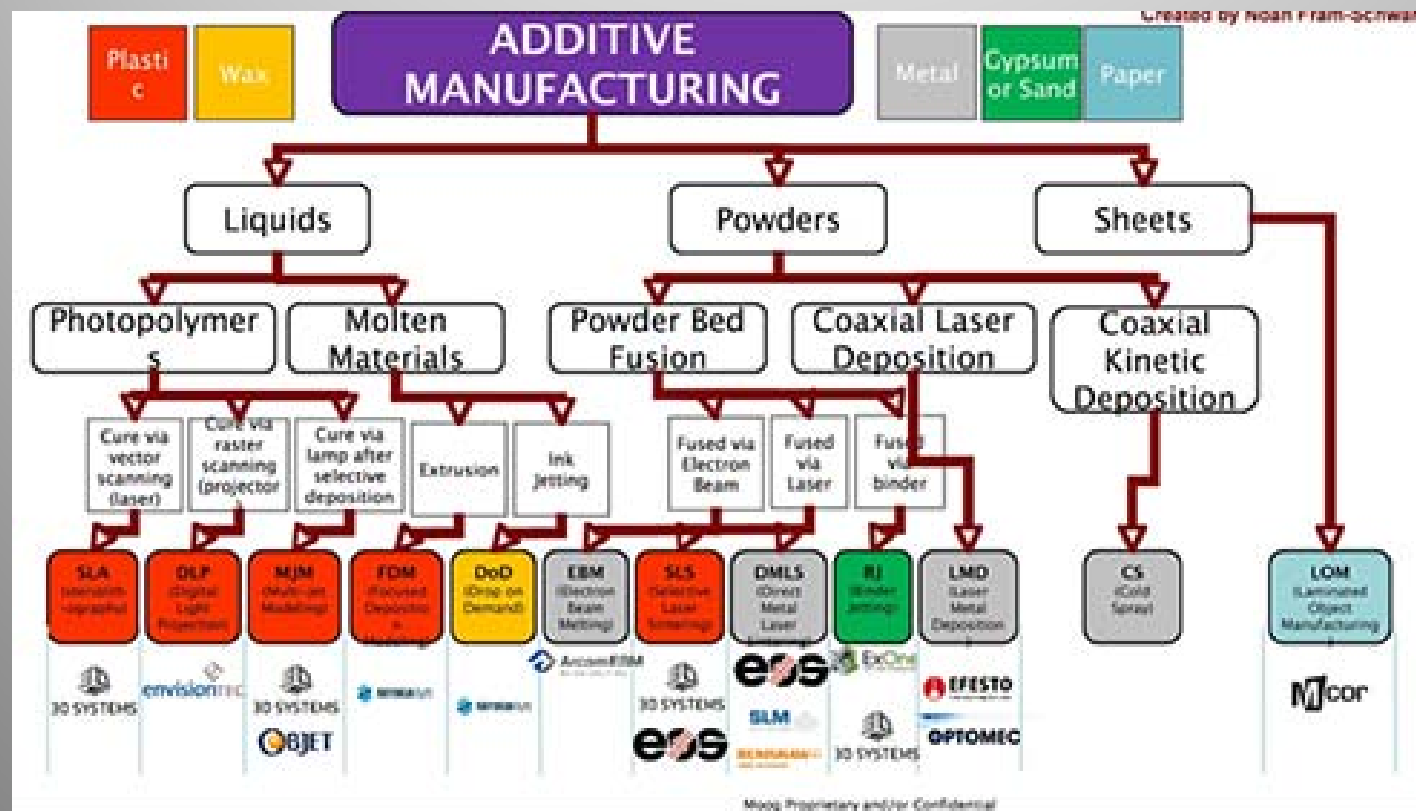
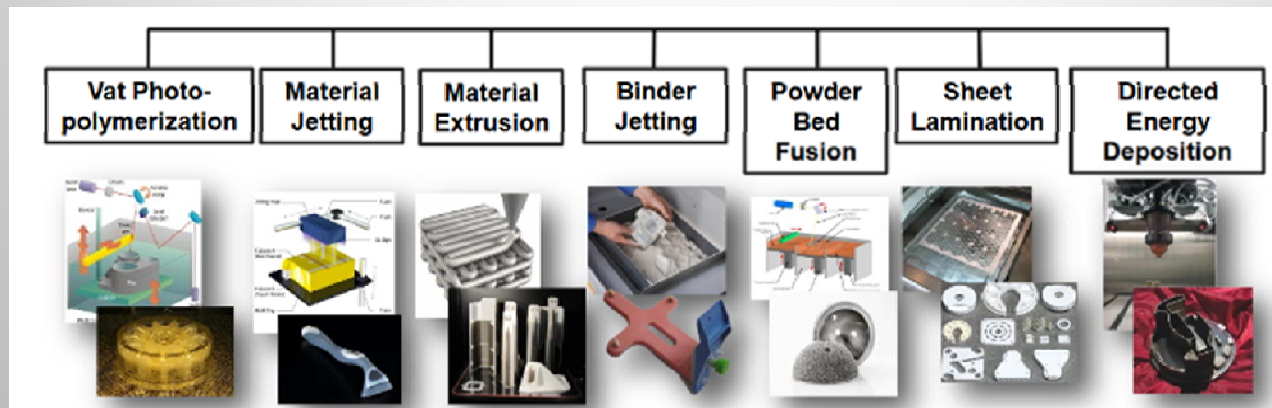
Digital Becomes Mainstream in Dentistry

ADDITIVE MANUFACTURING & 3D PRINTING

Additive Manufacturing Reshapes Patient's Face



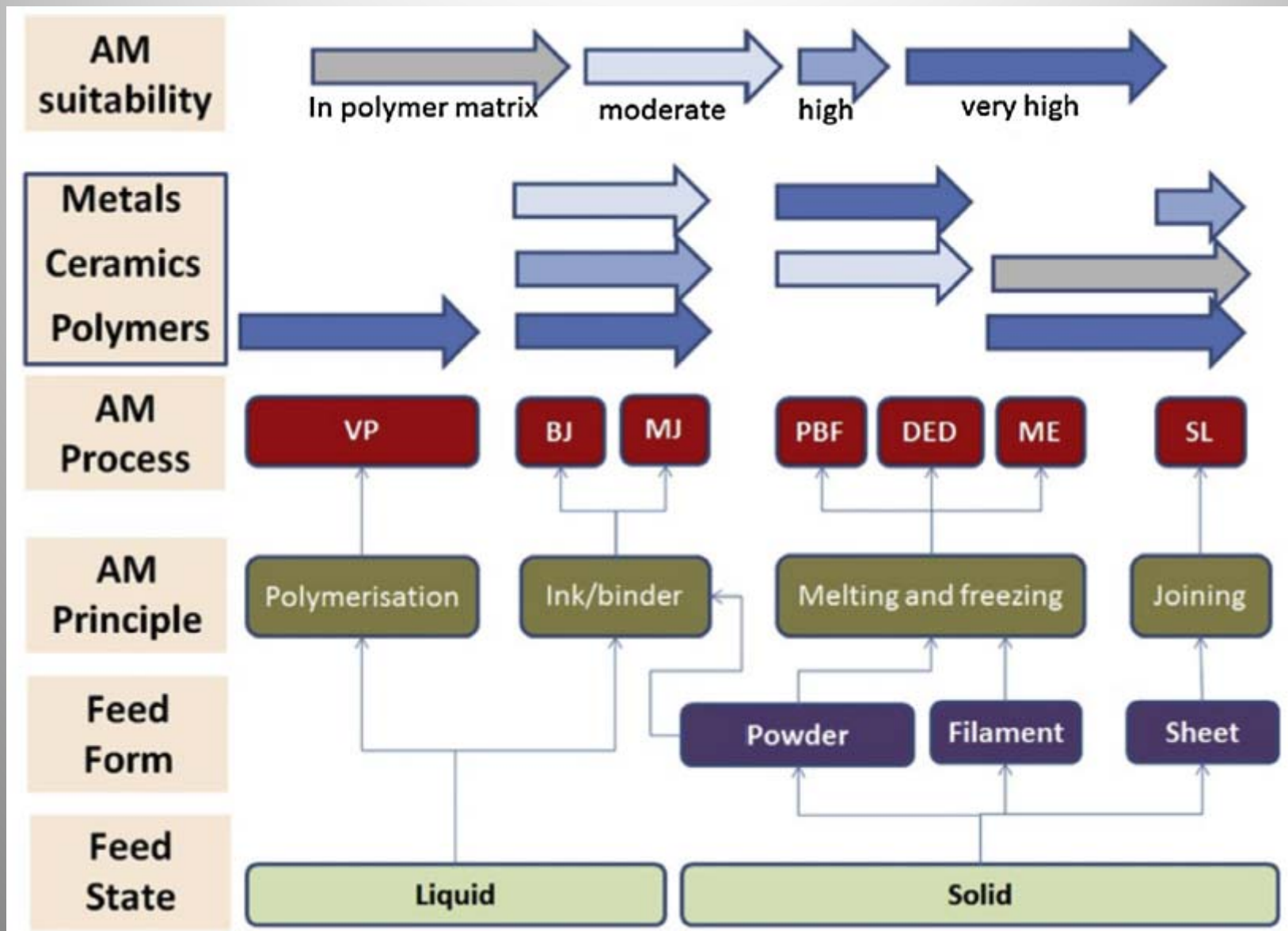
AM tehnologije



Karakteristike AM tehnologija

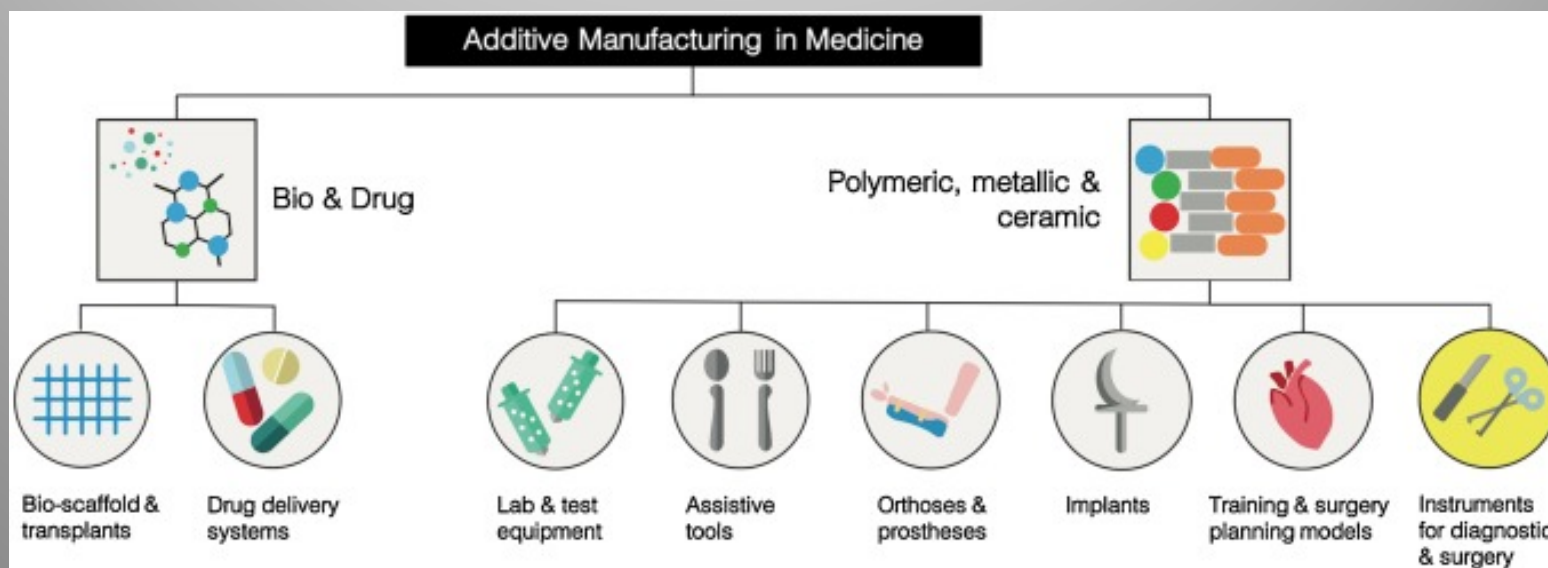
ASTM category	Basic principle	Example technology	Advantages	Disadvantages	Materials	Build volume (mm × mm × mm)	Tool manufacturer/country
BJ	Liquid binder/s jet printed onto thin layers of powder. The part is built up layer by layer By glueing the particles together	<ul style="list-style-type: none"> • 3D inkjet technology 	<ul style="list-style-type: none"> • Free of support/substrate • Design freedom • Large build volume • High print speed • Relatively low cost 	<ul style="list-style-type: none"> • Fragile parts with limited mechanical properties • May require post processing 	<ul style="list-style-type: none"> • Polymers • Ceramics • Composites • Metals • Hybrid 	Versatile (small to large) $X = <4000$ $Y = <2000$ $Z = <1000$	ExOne, USA PolyPico, Ireland
DED	Focused thermal energy melts materials <i>during</i> deposition	<ul style="list-style-type: none"> • Laser deposition (LD) • Laser Engineered NetShaping (LENS) • Electron beam • Plasma arc melting 	<ul style="list-style-type: none"> • High degree control of grain structure • High quality parts • Excellent for repair applications 	<ul style="list-style-type: none"> • Surface quality and speed requires a balance • Limited to metals/metal based hybrids 	<ul style="list-style-type: none"> • Metals • Hybrid 	Versatile $X = 600-3000$ $Y = 500-3500$ $Z = 350-5000$	Optomec, USA InssTek, USA Sciaky, USA Irepa Laser, France Trumpf, Germany
ME	Material is selectively pushed out through a nozzle or orifice	<ul style="list-style-type: none"> • Fused Deposition Modelling (FDM)/Fused Filament Fabrication (FFF), Fused Layer Modelling (FLM) 	<ul style="list-style-type: none"> • Widespread use • Inexpensive • Scalable • Can build fully functional parts 	<ul style="list-style-type: none"> • Vertical anisotropy • Step-structured surface • Not amenable to fine details 	<ul style="list-style-type: none"> • Polymers • Composites 	Small to medium $X = <900$ $Y = <600$ $Z = <900$	Stratasys, USA
MJ	Droplets of build materials are deposited	<ul style="list-style-type: none"> • 3D inkjet technology • Direct Ink writing 	<ul style="list-style-type: none"> • High accuracy of droplet deposition • Low waste • Multiple material parts • Multicolour 	<ul style="list-style-type: none"> • Support material is often required • Mainly photopolymers and thermoset resins can be used 	<ul style="list-style-type: none"> • Polymers • Ceramics • Composites • Hybrid • Biologicals 	Small $X = <300$ $Y = <200$ $Z = <200$	Stratasys, USA 3D Systems, USA PolyPico, Ireland 3Dinks, USA WASP, Italy
PBF	Thermal energy fuses a small region of the powder bed of the build material	<ul style="list-style-type: none"> • Electron beam melting (EBM) • Direct Metal Laser Sintering (DMLS) • Selective Laser Sintering/Melting (SLS/SLM) 	<ul style="list-style-type: none"> • Relatively inexpensive • Small footprint • Powder bed acts as an integrated support structure • Large range of material options 	<ul style="list-style-type: none"> • Relatively slow • Lack of structural integrity • Size limitations • High power required • Finish depends on precursor powder size 	<ul style="list-style-type: none"> • Metals • Ceramics • Polymers • Composites • Hybrid 	Small $X = 200-300$ $Y = 200-300$ $Z = 200-350$	ARCAM, Sweden; EOS, Germany; Concept Laser Cusing, Germany; MTT, Germany; Phoenix System Group, France; Renishaw, UK;Realizer, Germany; Matsuura, Japan, Voxeljet, 3Dsystems, USA
SL	Sheets/foils of materials are bonded	<ul style="list-style-type: none"> • Laminated Object Manufacturing (LOM) • Ultrasound consolidation/Ultrasound Additive Manufacturing (UC/UAM) 	<ul style="list-style-type: none"> • High speed, • Low cost, • Ease of material handling 	<ul style="list-style-type: none"> • Strength and integrity of parts depend on adhesive used • Finishes may require post processing • Limited material use 	<ul style="list-style-type: none"> • Polymers • Metals • Ceramics • Hybrids 	Small $X = 150-250$ $Y = 200$ $Z = 100-150$	3D systems, USA MCor, Ireland
VP	Liquid polymer in a vat is light-cured	<ul style="list-style-type: none"> • Stereo Lithography (SLA) • Digital Light Processing (DLP) 	<ul style="list-style-type: none"> • Large parts • Excellent accuracy • Excellent surface finish and details 	<ul style="list-style-type: none"> • Limited to photopolymers only • Low shelf life, poor mechanical properties of photopolymers • Expensive precursors/Slow 	<ul style="list-style-type: none"> • Polymers • Ceramics 	Medium $X < 2100$ $Y < 700$ $Z < 800$	Lithoz, Austria 3D Ceram, France

Karakteristike AM tehnologija



Primena AM tehnologija u medicini/stomatologiji

1. Edukacija (doktori, pacijenti, forenzičari) i izrada medicinskih/anatomskih modela.
2. Personalizovano predhirurško lečenje i predoperativno planiranje.
3. Fabrikovanje tkiva i organa, sintetički organi za ispitivanje lekova
4. Izrada personalizovanih proteza, implanta, medicinskih pomagala, vođica, membrana, i sl.
5. Proizvodnja hiruških i dijagnostičkih instrumenata, uređaja i sl.
6. Primena u farmaciji – razvoj novih lekova, novi forme doziranja, novi načini isporuke lekova i sl.



Primena AM tehnologija u medicini/stomatologiji

(oblast primene, ciljevi, benefiti)

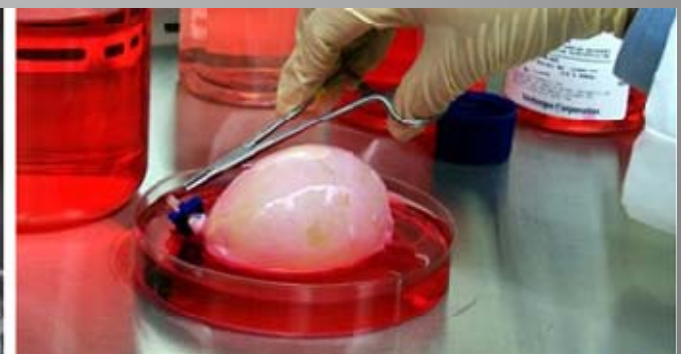
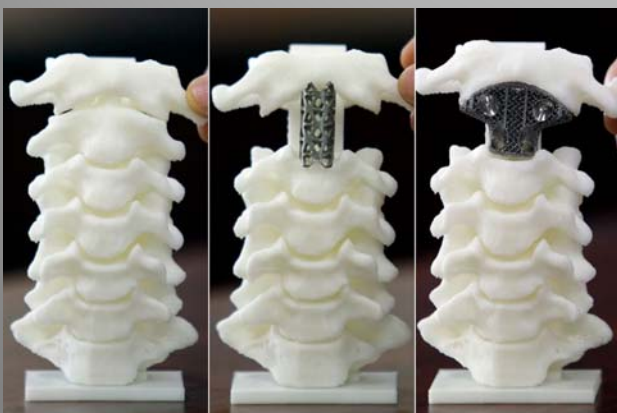
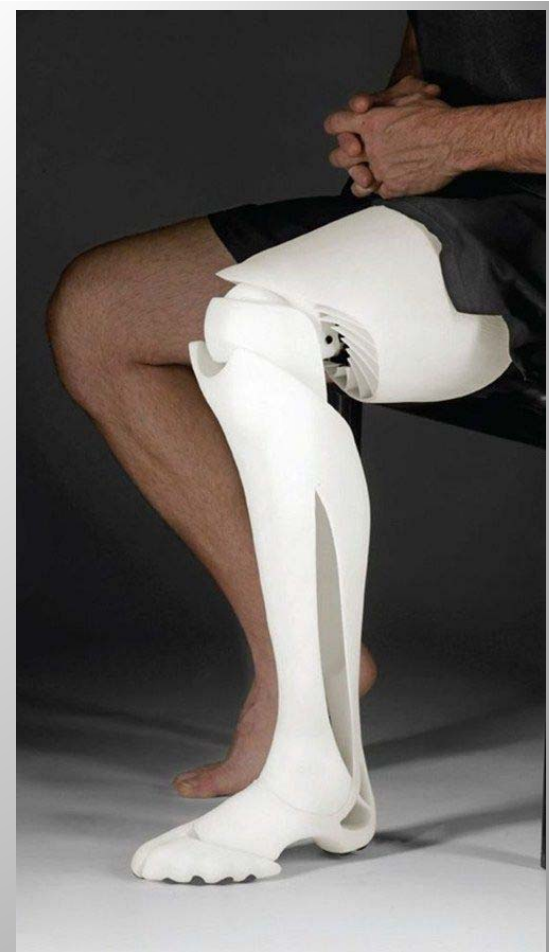
Major medical areas where Additive Manufacturing has been implemented.

S. no.	Area of medical application	Objectives	Major benefits
1	Surgical planning	<ul style="list-style-type: none"> The main objective is how AM become more beneficial in surgical planning These models provide surgical and physician team a visual aid used to become surgery planning better Bone structure of patient is studied before surgery, which reduced operation time, cost as well as risk 	<ul style="list-style-type: none"> With the help of this technology during operation, we predicted the problem cause and obtained diagnostic quality AM models are better understood the complex anomaly and complicated procedure These models especially help in surgeries where there are deformities or anatomical abnormalities, in surgery of heart surgery of spine maxillofacial and craniofacial surgery
2	Medical education and training	<ul style="list-style-type: none"> The primary purpose is that how this technology provides better demonstration of internal and external human anatomy structure It consists of many colours, so these models are used in teaching as well as in research purpose in medical education 	<ul style="list-style-type: none"> AM models used for better illustration in school and museums These models are used by young doctors or medical students to understand surgical procedure and problem without causing patient in discomfort
3	Design and development of devices and instrumentation used in medical	<ul style="list-style-type: none"> The purpose of this technology is how this helps for design and development of devices and instrumentation used in medical 	<ul style="list-style-type: none"> For fabrication of medical devices and instrumentation AM is used because this technique design the model, develop and then produced required medical equipment or instruments It includes hearing aid, dental devices and surgical tools
4	Customised implant design	<ul style="list-style-type: none"> The purpose of this technology has potential to fabricate customised fixtures and implants Complex geometry is also built in short time 	<ul style="list-style-type: none"> CAD and AM technology make possible to manufacture customised implants which comfortably fit the patient with reasonable cost AM create accurate implant for patient rather than standard-sized implants such as knee joints, spinal implant and dental implant which is significantly beneficial for patient Surgical implant become more precise by using AM

Primena AM tehnologija u medicini/stomatologiji

(oblast primene, ciljevi, benefiti)

S. no.	Area of medical application	Objectives	Major benefits
5	Scaffoldings and tissue engineering	<ul style="list-style-type: none"> The primary purpose is how this technology fabricates implant with its unique geometrical characteristics like scaffolds for the restoration of tissues It replaces conventional scaffold fabrication methods 	<ul style="list-style-type: none"> With customised implant fabrication risk and surgery time is reduced The scaffold is supporting structure and provides support and guidance to defective patient bone or growing tissue which is damaged AM techniques like FDM, SLS and 3D printing are suitable for fabricating controlled porous structures by using application of biomaterial contributing in the field of tissue engineering and scaffolding AM technology increased the ability to produce complex geometry product with higher accuracy
6	Prosthetics and orthotics	<ul style="list-style-type: none"> How this technology is beneficial in prosthetics and orthotics field of Medical which starts with particular patient anatomy 	<ul style="list-style-type: none"> Accurate alignment characteristics of patient also needed in this model, which allowing biomechanically correct geometry development and improves comfort, stability AM fabricate custom prosthesis which fit precisely to patient at reasonable cost such as pattern of dental crowns
7	Mechanical bone replicas	<ul style="list-style-type: none"> How AM technology used for mechanical bone model fabrication This technology replicates the material variation done easily 	<ul style="list-style-type: none"> SLA can create composite structure which has similar property of bone These bones can be provided strength under various conditions Also beneficial to recreate the stresses, fractures and different changes in bone, which give more helps to researcher and doctors
8	Forensics	<ul style="list-style-type: none"> AM tool is more beneficial tool for investigation of criminal, such as homicide cases where crime scene for investigation reconstructed 	<ul style="list-style-type: none"> These models kept evidence for investigation of criminal and manufacture of different scaffolds investigator in finding some question answer In many cases, it is used to create events and scene accurately which quickly help for solving cases



AM tehnologije u medicini

Postupak	Materijal	Primena
Polimerizacija u kadi (SLA, DLP, TFSLA)	Polimerna smola	Veštačke kosti, dentalni modeli i implantati, vođice, slušni uređaji
Fuzija praškastog supstrata (SLS, DMLS, EBM, SLM)	SLS: Polimeri (PLA, PC, ABS..) DMLS, EBM, SLM: Metali (nerđajući čelik, titanijum, aluminijum, legirani čelik-Cr, bakar)	Medicinski modeli, medicinski aparati, implantati, proteze, fiksatori...
Brizganje vezivnog sredstva (3DP)	Metali: nerđajući čelik Polimeri: ABS, PA, PC Keramika: staklo	Modeli u boji, posebno modeli za kodiranje anatomije u boji
Brizganje materijala (MJM, PJ)	Polimeri: PP, HDPE, PS, PMMA, PC, ABS, HIPS, EDP	Medicinski modeli, dentalni odlivci, vođice dentalnih implanata
Ekstrudiranje materijala (FDM, FFF)	Polimeri: ABS, nylon, PC, AB	Medicinski instrumenti i uređaji, exoskeleton
Laminacija folija (LOM)	Papir, plastika, lim	Ortopedsko modelovanje površine kostiju
Direktno energetska taloženje (DED, LMD)	Metali: kobalt, hrom, titanijum	Reparacija postojećih uređaja i komponenti, izrada delova većih dimenzija

AM materijali u medicini i stomatologiji

- Akrilni fotopolimeri
- Metali (nerđajući čelik, titnijum i legure titanijuma, kobalt, hrom I legure na bazi hroma, leguremagnezijuma, aluminijum, bakar)
- Napredni biokeramički materijali (glinica, cirkonijum, biokeramika na bazi kalcijum fosfata, porozna keramika itd.)
- Polimerno-keramički kompozitne rešetke (scaffold) od polipropilen-trikalcijum fosfata (PP-TCP). PCL i PCL-hidroksiapatit (HA) za FDM, PLGA, polimere na bazi skroba, scaffold na bazi polikaprolaktona (PCL) i polietereeterketonehidroksiapatit (PEEK-HA) za bioprinting
- Vezivno sredstvo u prahu - kalcijum fosfat poznat kao koštani cement, koji je mešavina tetrakalcijum fosfata (TTCP) i beta trikalcijum fosfata (TCP) i sličnih materijala, polimetilmetakrilat (PMMA), polimerni kompoziti kalcijum fosfat cementa za zamenu kostiju i hrskavice, implantati i proteze .

1984

- **Charles Hull** invented *Stereolithography*

1996

- **Dr. Gabor Forgacs** observed that *cells stick together during embryonic development*
- (*Dr Gabor Forgacs primetio je da se ćelije drže zajedno tokom embrionalnog razvoja*)

2000

- Urinary bladder augmentation using a *synthetic scaffold* seeded with the patients' own cells
- (Povećanje mokraćne bešike pomoću sintetičke rešetke (scaffold) posejane sopstvenim ćelijama pacijenata)

2003

- **Thomas Boland's lab** modified an *inkjet printer* to accommodate and dispense cells in scaffolds
- (Laboratorija Tomasa Bolanda modifikovala je inkjet štampač za deponovanje ćelija na scaffold rešetku)

2009

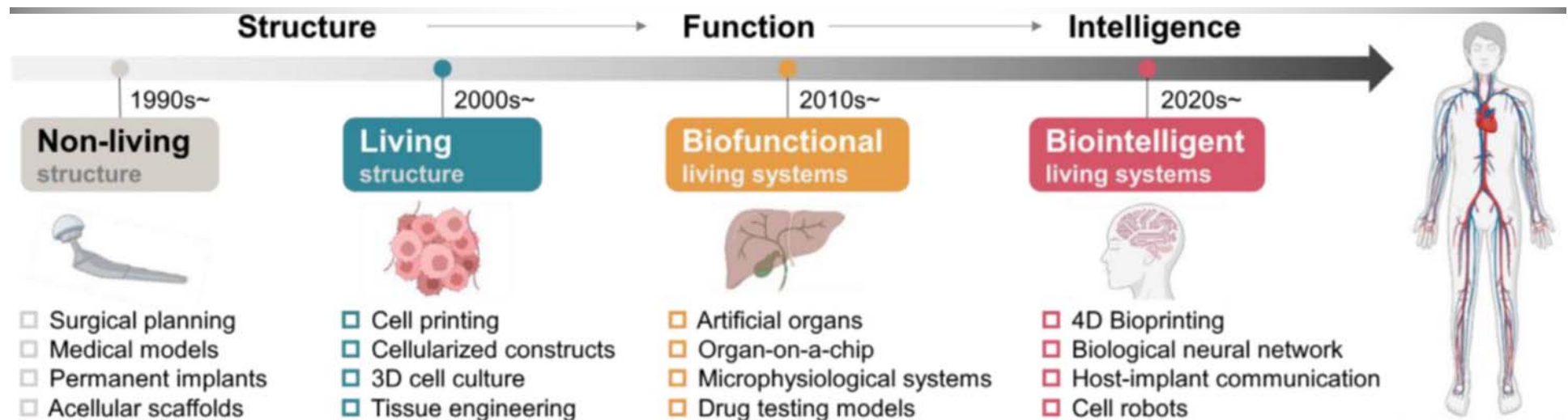
- Organovo, creates the *NovoGen MMX Bioprinter* using Forgacs technology
- (Kompanija Organovo razvila NovoGen MMKS Bioprinter koristeći Forgacs tehnologiju)

2010

- Organovo prints the first human blood vessel without the use of scaffolds
- (Organovo štampa prvi ljudski krvni sud bez upotrebe scaffold-a)

2011

- Organovo develops 3D bioprinted disease models made from human cells.
- (Organovo razvija 3D bioštampane modele abnormalnih stanja napravljene od ljudskih ćelija)



Orthopedic innovations over time

The decade of the 1970s is known for the metal joint replacement, the 1980s computer-assisted surgery, the 1990s the widespread use of arthroscopy, and the 2000s tissue engineering. This decade will likely be known for robotic surgery, distance surgery and virtual reality training, which is already in widespread use in teaching tomorrow's orthopedic surgeons.

1970s

Metal joint replacement

1980s

Computer-assisted surgery

1990s

Arthroscopy

2000s

New tissue innovation

2010s
and beyond

Robotics,
3D printing,
personalized implants

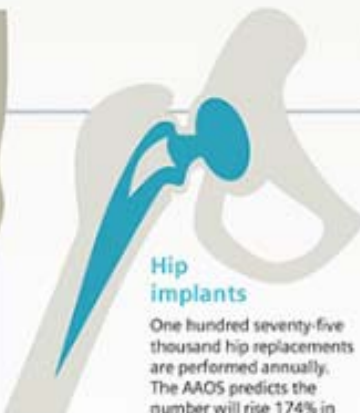
Knee implants

A half-million knee replacements are performed annually. The American Academy of Orthopaedic Surgeons (AAOS) predicts the number will rise 673% in the next twenty years.



Hip implants

One hundred seventy-five thousand hip replacements are performed annually. The AAOS predicts the number will rise 174% in the next twenty years.



Varieties of personalization

Surgical robots and computer-assisted surgical tools:

- Cutting guides
- Navigation
- Haptic feedback
- Implant placement

Custom implants:

- Knee
- Hip
- Spinal
- Ankle
- Shoulder
- Maxillofacial



Spinal implants

BioPrinting / BioFabrikacija (Tissue engineering)

- Kompjuterski podržan bio-additivni proizvodni proces kojim se deponuju žive ćelije zajedno sa skeletom (scaffold), u cilju fabrikacije tkiva i organa.
- Koristi tehnologiju štampe 3D za proizvodnju ćelija, biomaterijala i biomaterijala od samih ćelija pojedinačno ili u tandemu, sloj po sloju, direktno stvarajući 3D strukture tkiva.
- Na raspolaganju su različiti materijali za izgradnju skeleta (scaffold), u zavisnosti od željene čvrstoće, poroznosti i vrste tkiva, sa hidrogelima koji se obično smatraju najpogodnijim za proizvodnju mekih tkiva.
- Koriste se različite bioadditive tehnologije proizvodnje, uključujući:
 - Laser-based writing,
 - Inkjet based printing ,
 - Extrusion-based deposition

Bioprinting na bazi inkjeta/ekstruzije je najviše zastupljen!!!

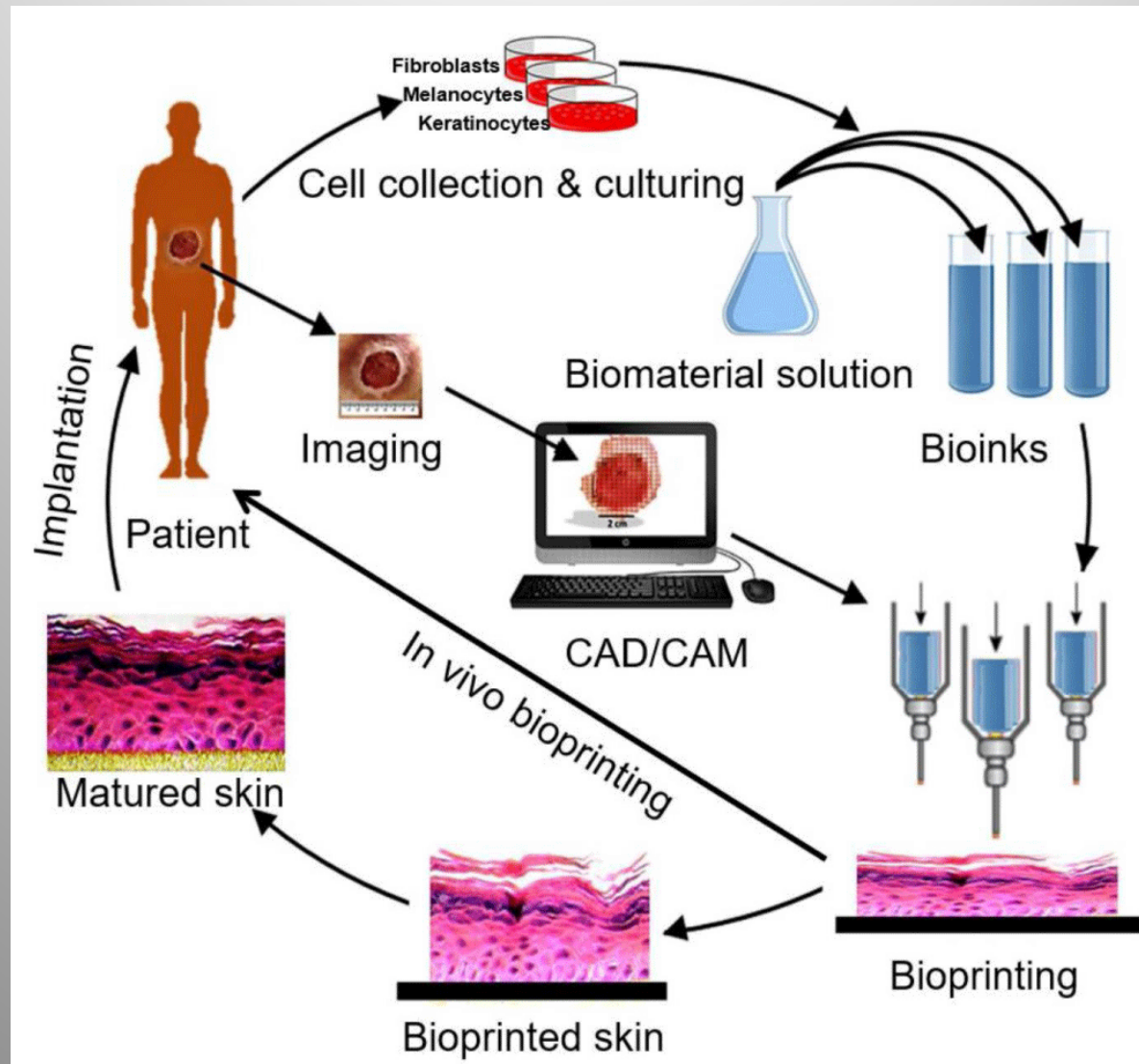
- Bioprinting omogućava veliku preciznost u pogledu prostornog deponovanja ćelija.
- Precizno pozicioniranje više vrsta ćelija je neophodno za izradu gustih i složenih organa, kao i za istovremenu konstrukciju integrisanog vaskularnog ili mikrovaskularnog sistema koji je od ključnog značaja za funkcionisanje organa

BioPrinting / BioFabrikacija (Tissue engineering)

Faze (koraci) u bioprintingu:

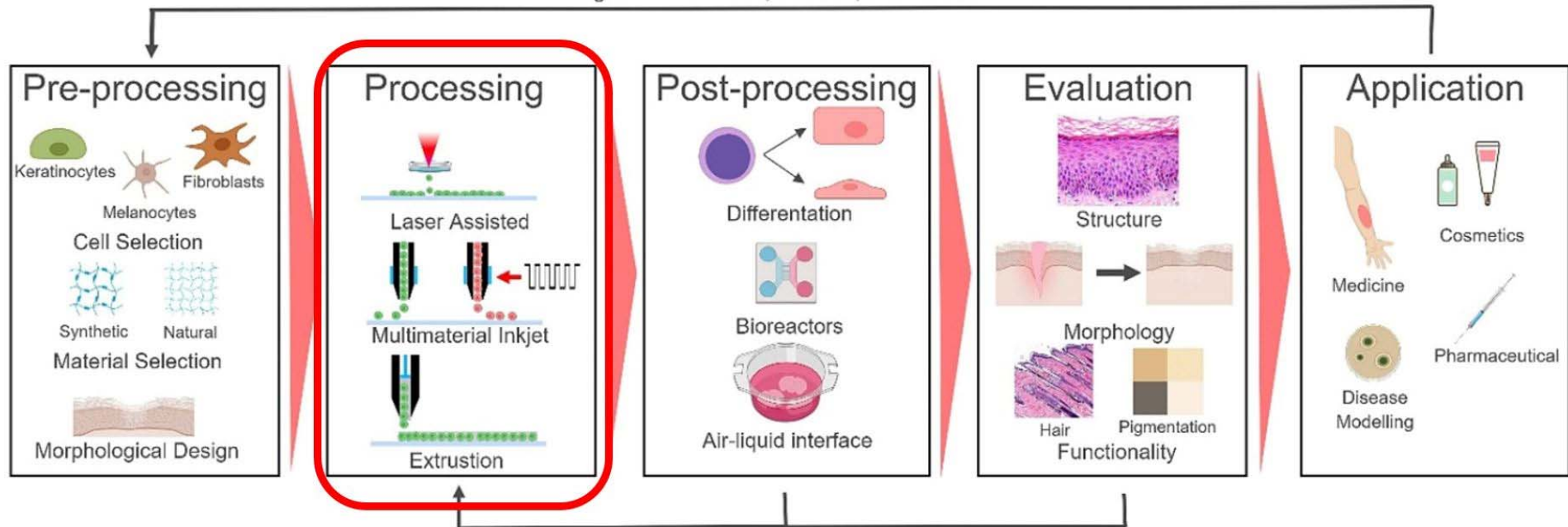
- 1) kreiranje strukture-šeme (blueprint) organa zajedno sa vaskularnim sistemom
- 2) generisanje plana procesa 3D bioprintinga;
- 3) izolacija matičnih ćelija;
- 4) diferencijacija matičnih ćelija u ćelije organa;
- 5) priprema bioink rezervoara sa specifičnim ćelijama organa, ćelijama krvnih sudova i potpornih struktura i pozicioniranje istih u Bio-šampač;
- 6) bioprint;
- 7) postavljanje bio-printovanog organa u bio-reaktor pre transplantacije.

BioPrinting / BioFabrikacija (Tissue engineering)

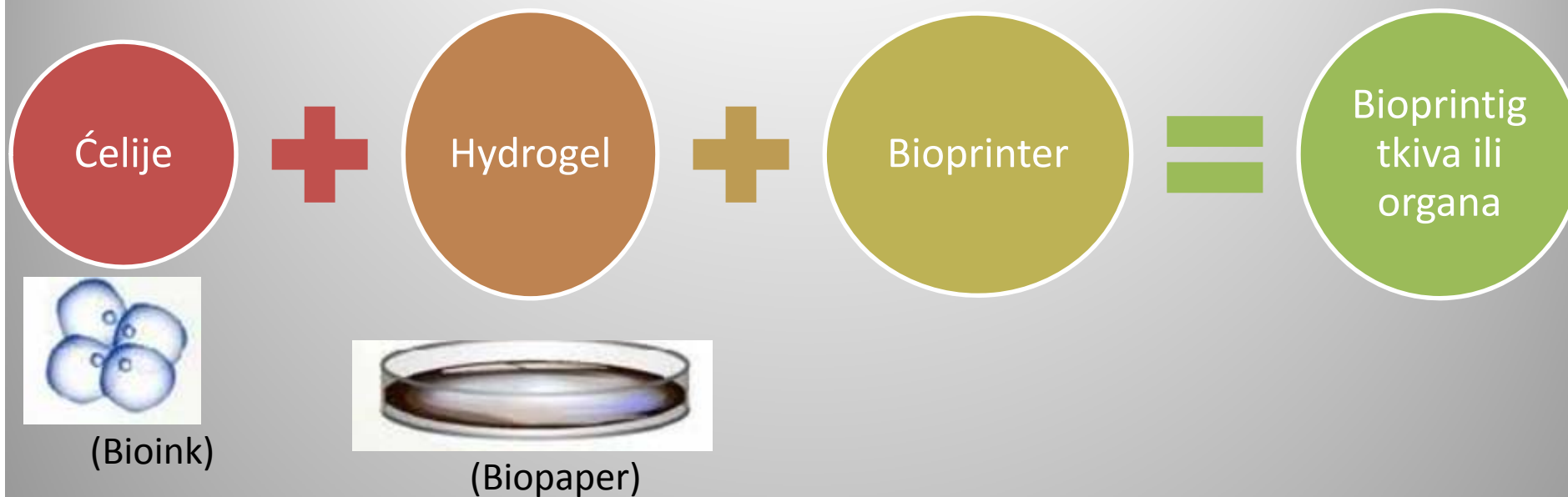


BioPrinting / BioFabrikacija (Tissue engineering)

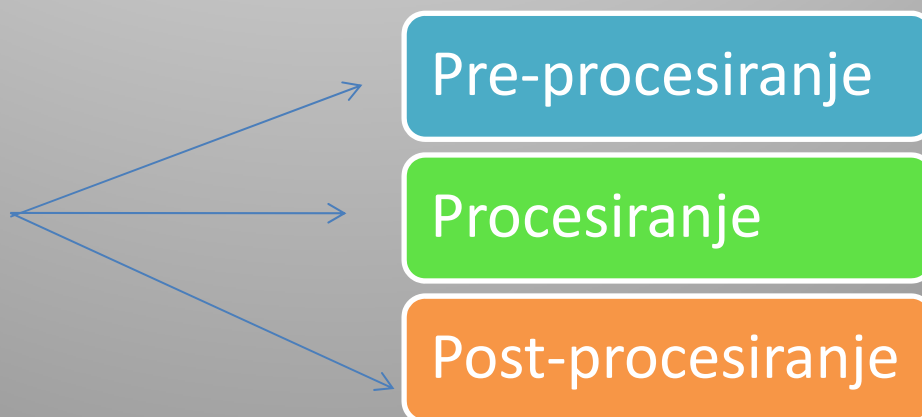
Autologous cell donation, 3D scan, diseased cell lines



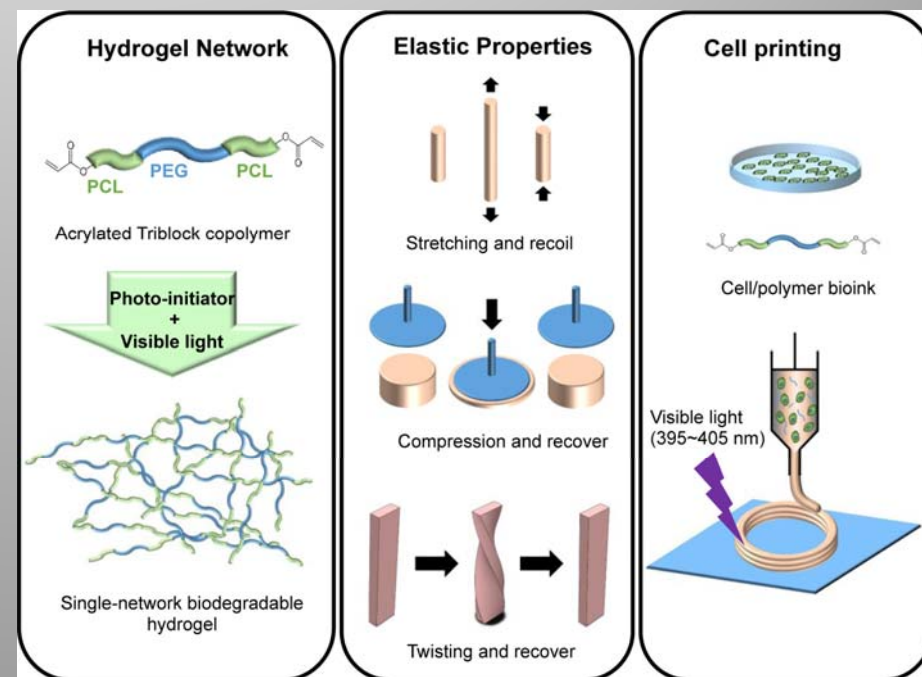
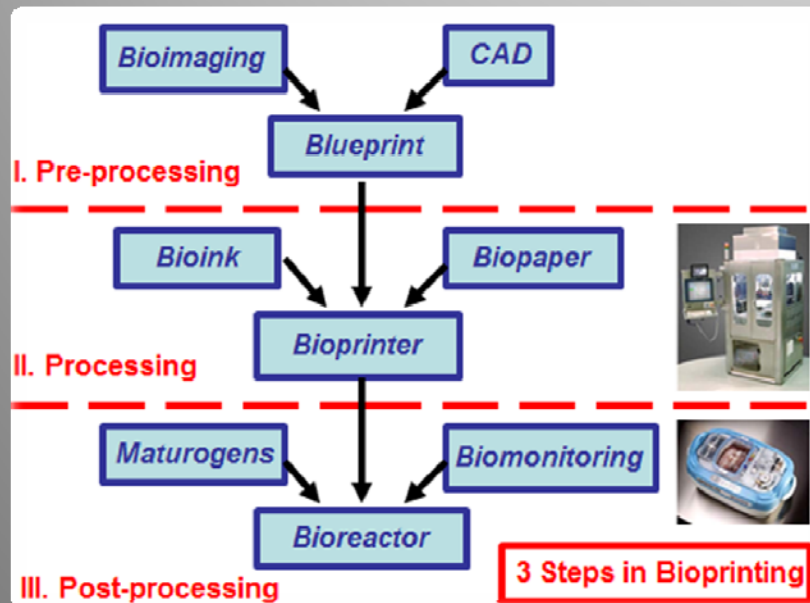
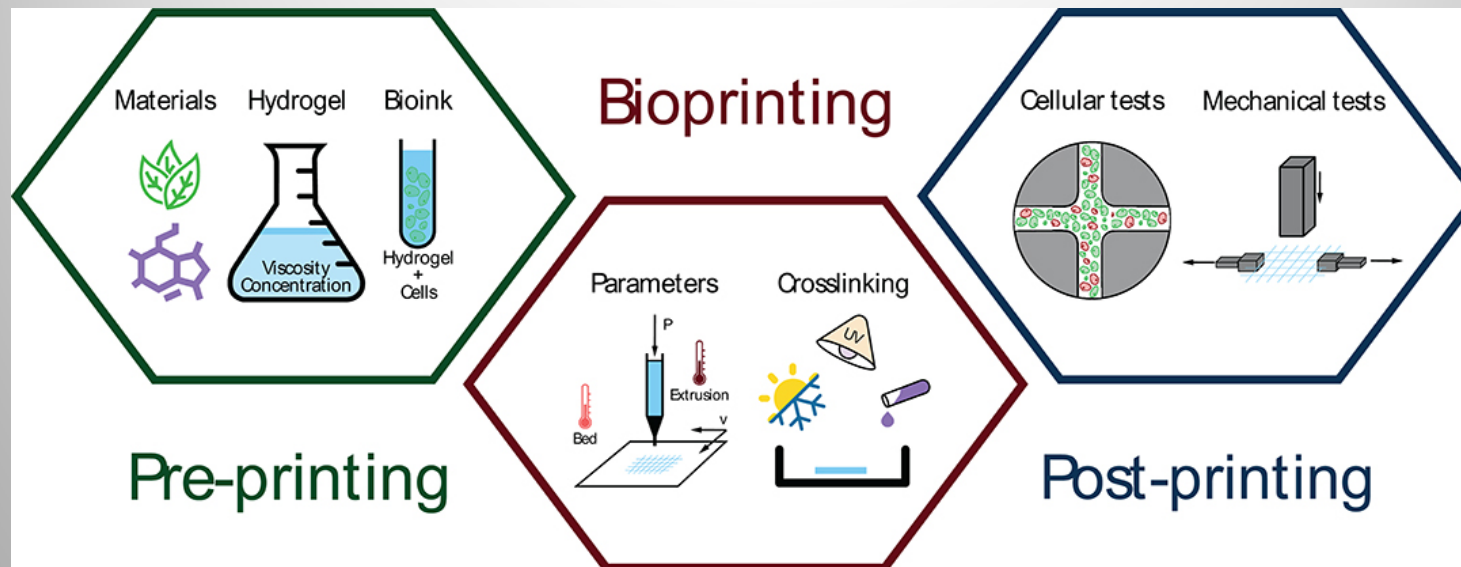
Komponente neophodne za bioprinting



3 faze



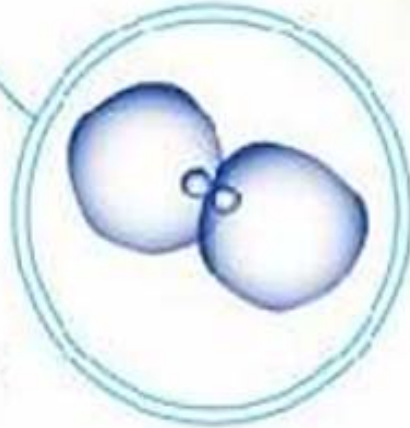
Komponente neophodne za bioprinting



Kreiranje Bioink-a

1 Cells

Poreklo: ćelije pacijenta dobijene biopsijom ili matične ćelija. Uzgajane standardnim metodama i tehnikama.

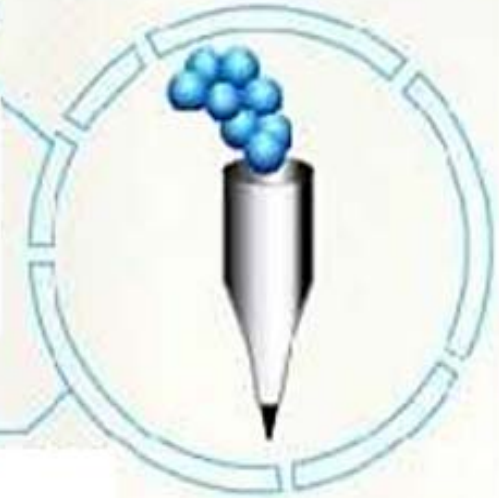


3 Collected

Kada se proizvede dovoljno ćelija, sakupljaju se da bi se napravio Bio-Ink.

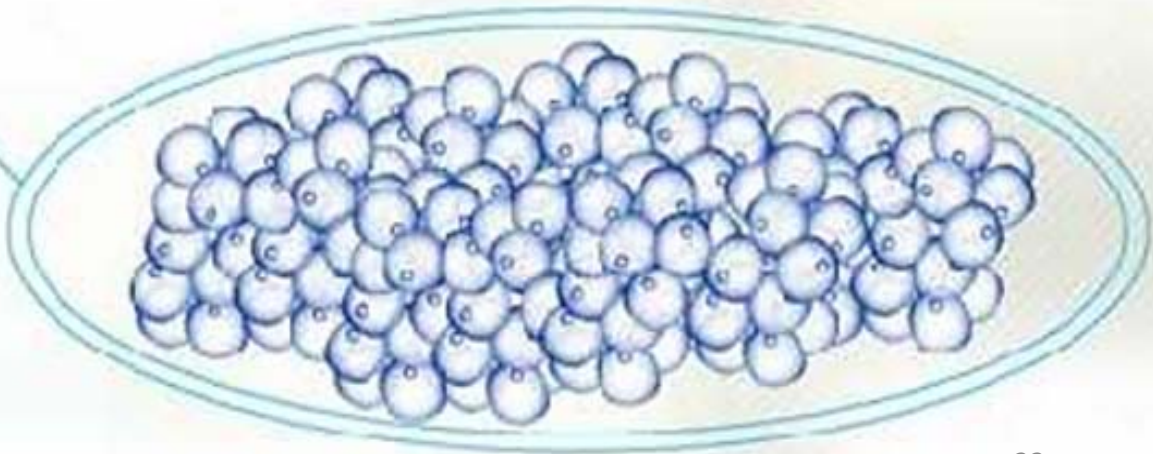
CELLS ARE THEN

- Sferoidni oblik
- Unošenje u kertridž radi kreiranja Bio Ink-a.



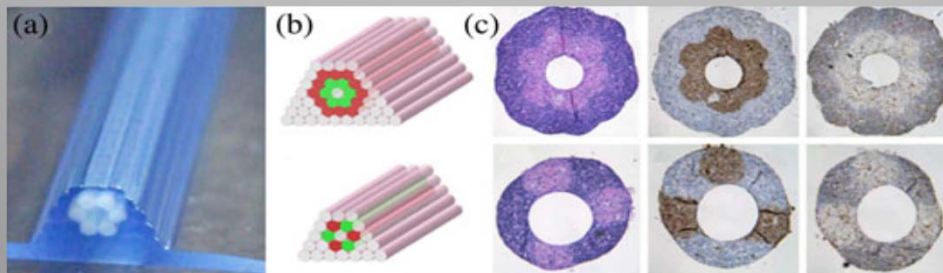
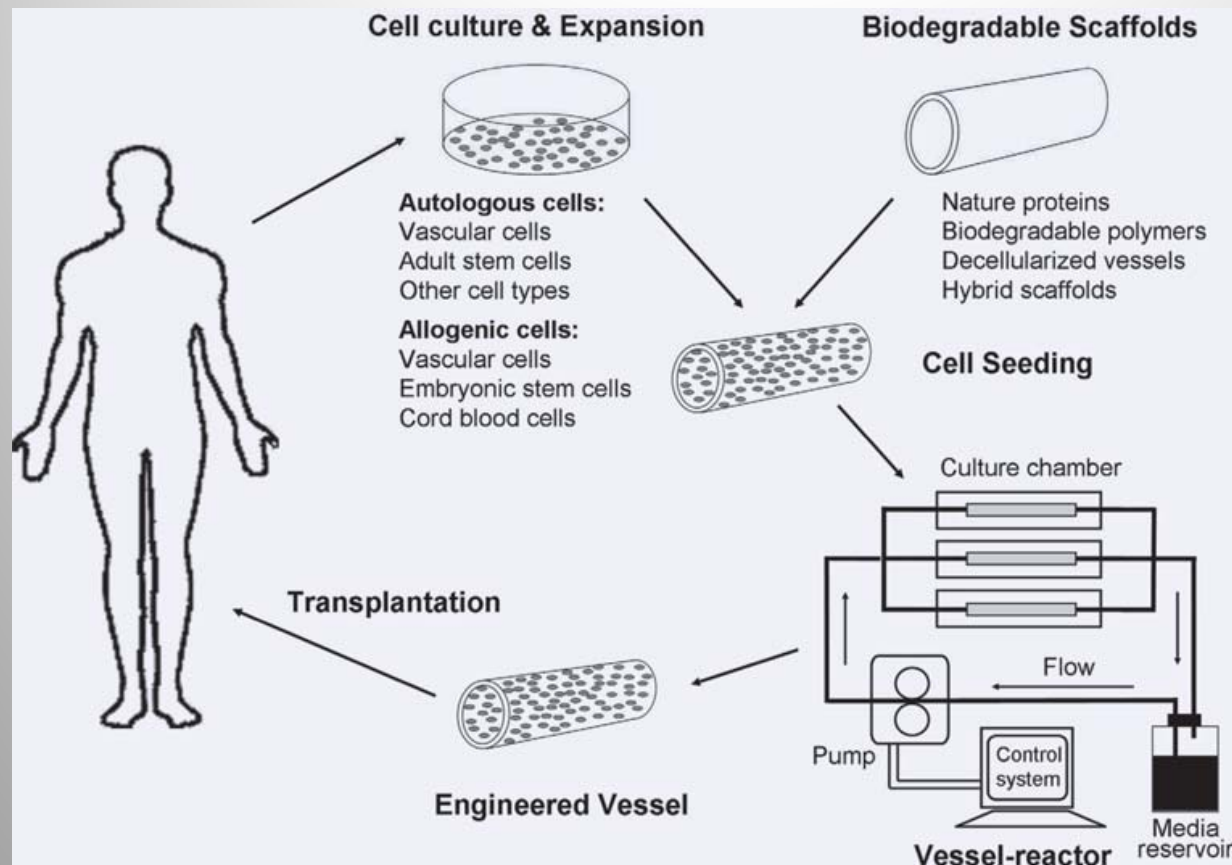
2 Cultured

Ćelije se uzgajaju u mediju za rast što omogućava ćelijama da se množe i rastu.





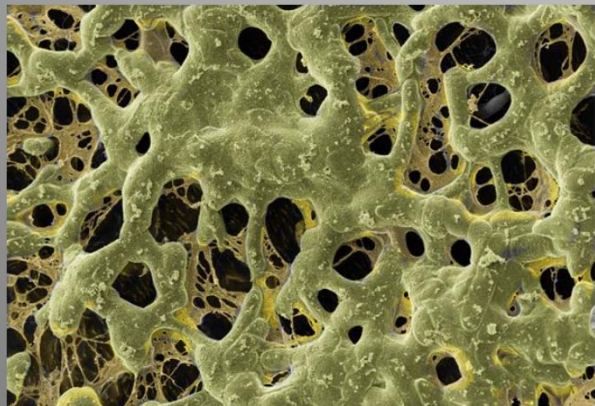
Bioprinting krvnih sudova



Tkivni sferoidi za štampanje krvnih sudova: (a) taloženje ravnih niti koje sadrže niz tkivnih sferoida (obojenih belom bojom) sa agaroznim (polisaharidnim) filamentima kao pomoćnim materijalom (obojeno u plavo) oko ćelijskih filamenata i unutar jezgra, (b) dizajn za višćelijski sklop sa (c) štampanim uzorcima sa ćelijama glatkih mišića pupčane vene i ćelijama fibroblasta kože.

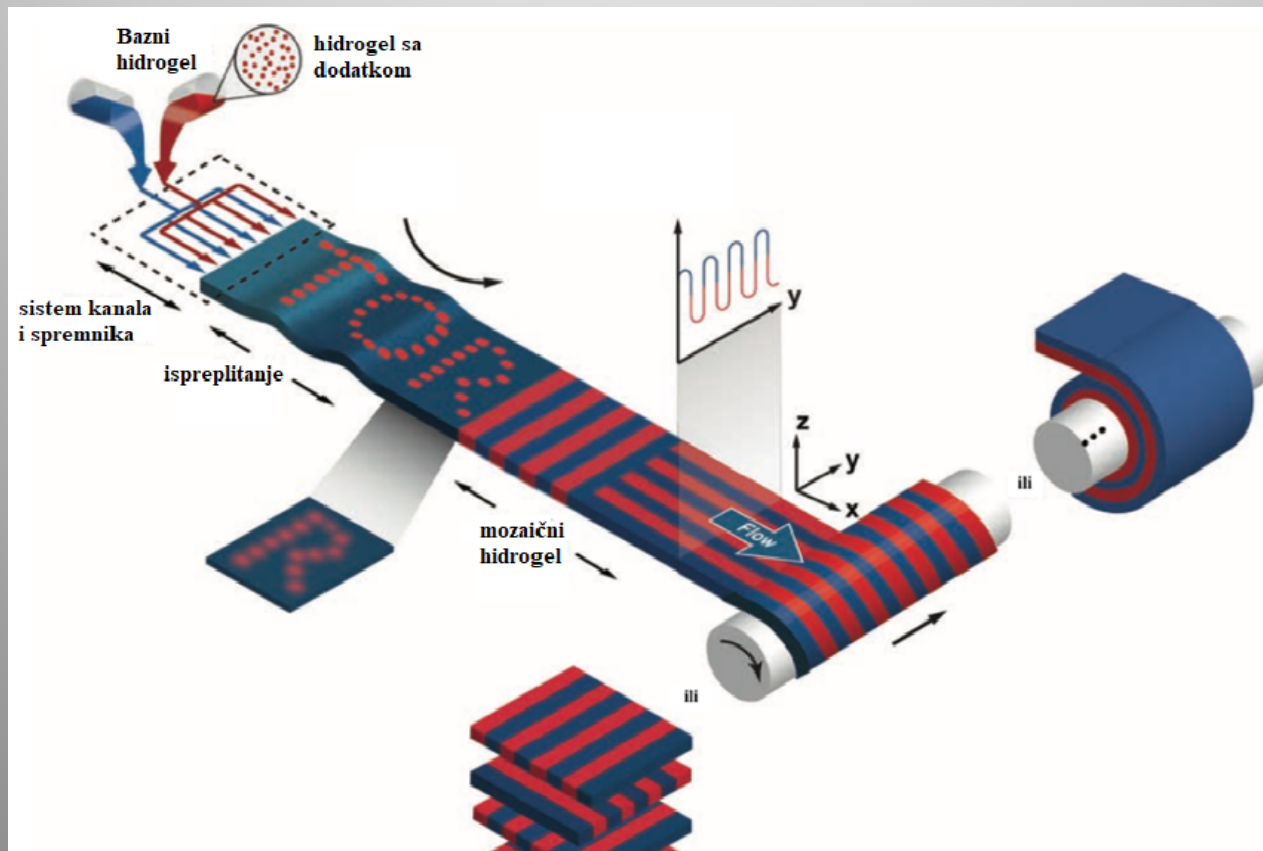
Hidrogel

- Glavni cilj inženjerstva tkiva je pronaći odgovarajuću podlogu koja bi bila analogna prirodnoj izvanćelijskoj matrici.
- Problem koje se javlja prilikom slojevitog štampanja ćelija, posebno u strukturama većih dimenzija jeste brzo raspadanje takve strukture zbog nedostatka krvnih sudova za dovod kiseonika i hranjivih materija.
- **Hidrogel** je biorazgradivi materijal koji u štampanom obliku daje formu, zajedno sa ćelijama suspendovanim u mastilu na bazi vode, te biorazgradivom polimeru raspoređenom u rešetkastom uzorku i privremenoj strukturi.
- Tkivo ima sistem mikrokanala koji omogućuje da se hranjive materije i kiseonik iz tela rasprši u strukturu dok se sistem krvnih sudova ne formira
- Hidrogel je supstanca koja nastaje kada organski polimer (prirodni ili veštački) počne gelirati kako bi stvorio trodimenzionalnu otvorenu rešetku koja hvata molekule vode ili druge rastvore pomoću kojih nastaje gel. Može da absorbuje veliku količinu vode ili biološkog fluida (suspenzije).

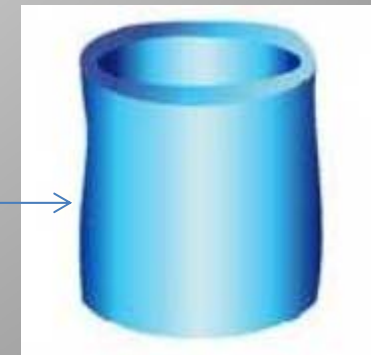
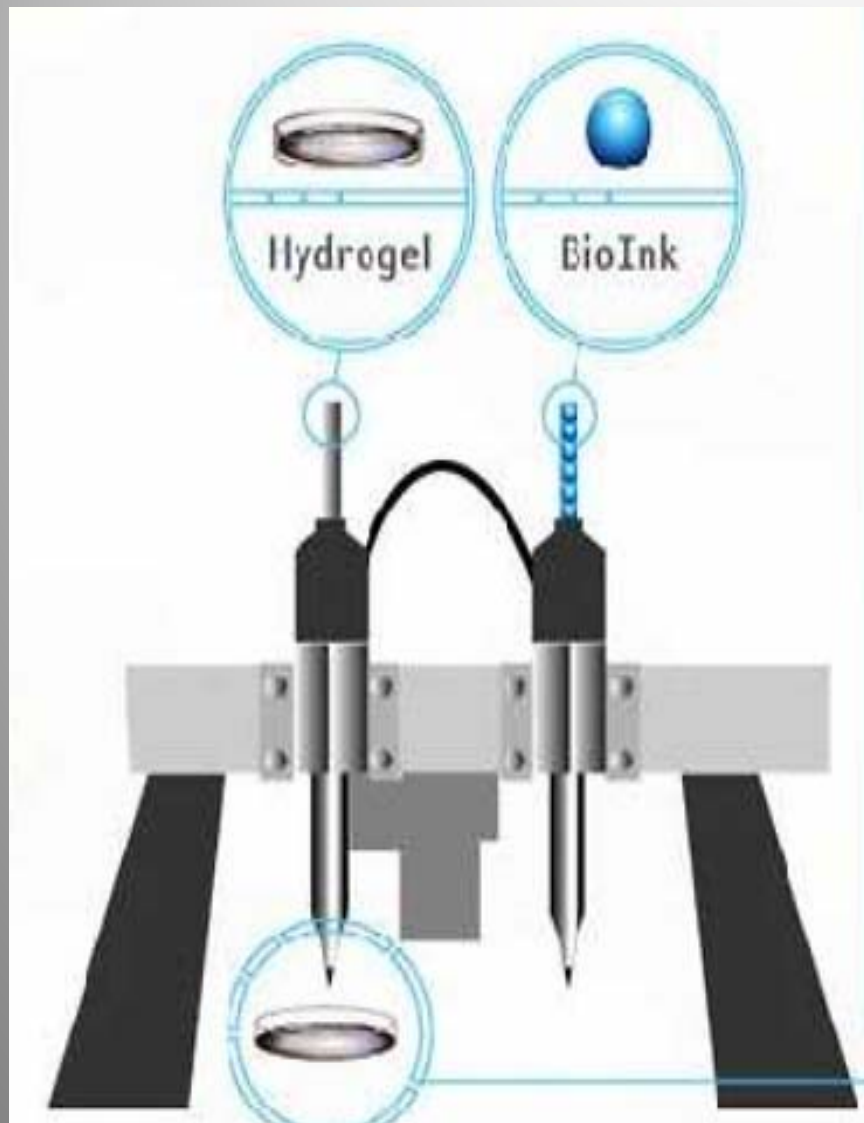


Štampanje/nanošenje hidrogela

- Stvaranje slojevite strukture vrši se ispreplitanjem mekih biopolimernih slojeva na način da se kroz jedan biopolimer koji predstavlja bazu, provlači drugi koji ima osobinu da u sebi može sadržavati mikročestice, biomolekule ili žive ćelije.
- Rastvori dva različita biopolimera odvojeni su u različitim spremnicima.
- Nizom kanala dovode se do izlaza na kojem počinje njihovo ispreplitanje (stvaranje mozaika).
- Slaže se oko deset različitih slojeva od milimetra do centimetra dužine koji sadrže praznine, područja spajanja slojeva i područja popunjena mikročesticama (npr. ćelijama)-

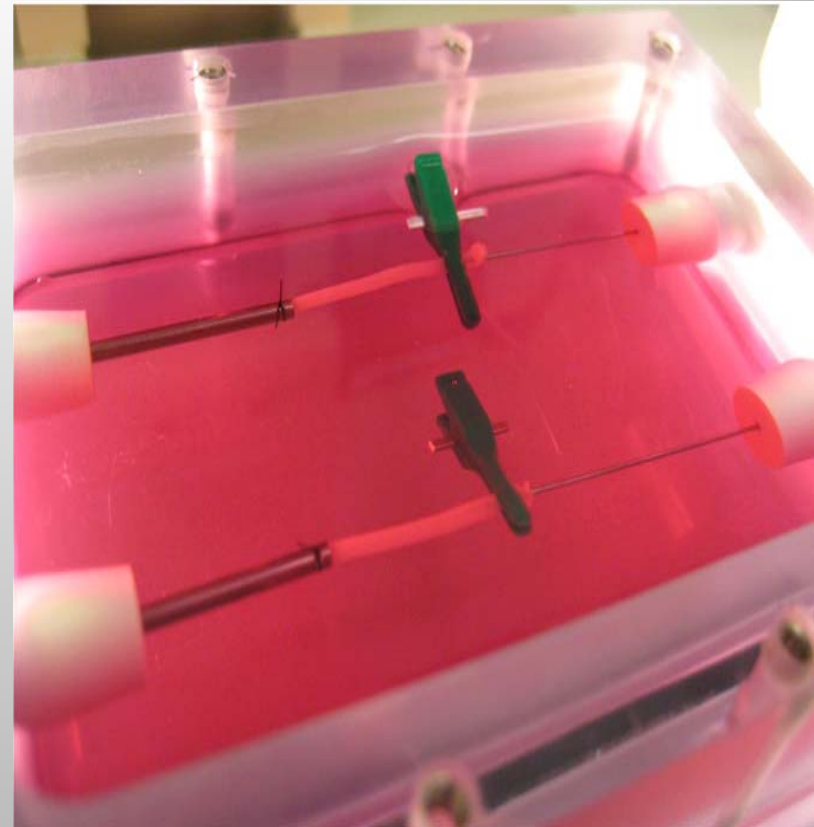


Proces štampanja



Sazrevanje

Post-printing

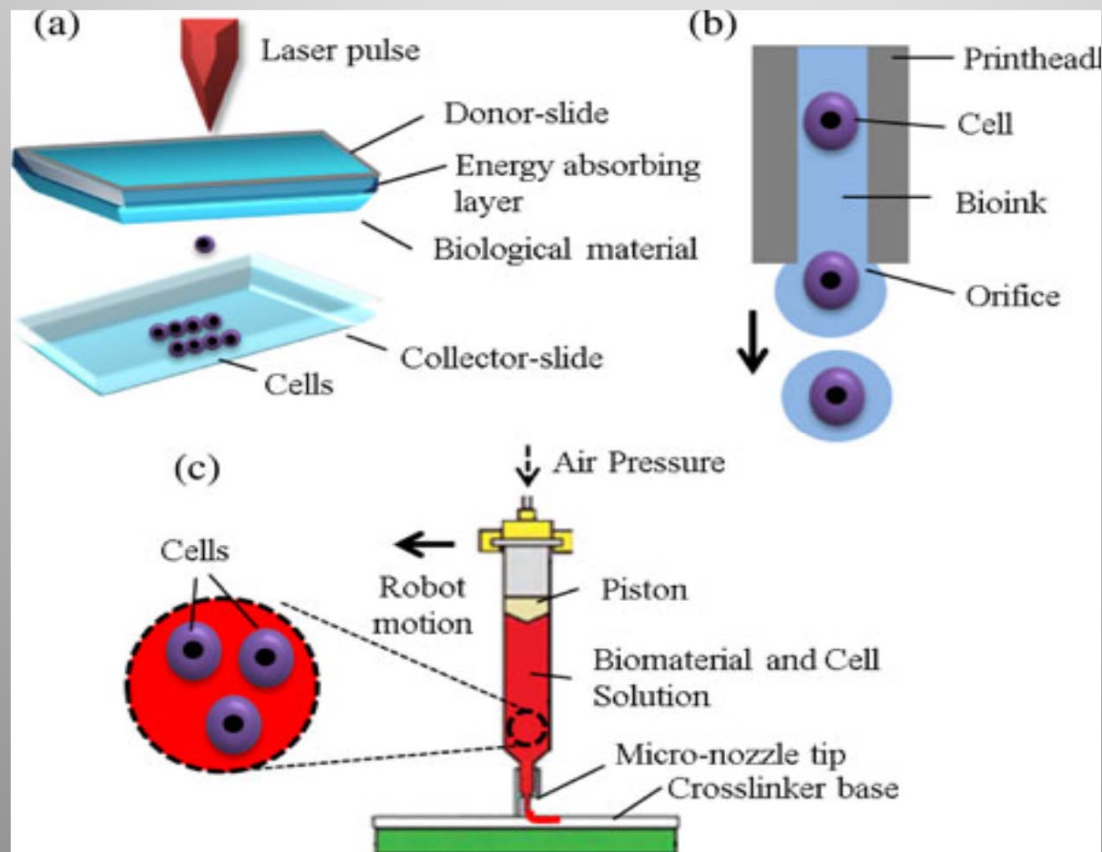


Bio-Reaktor za post-printing sazrevanje fabrikovanog krvnog suda

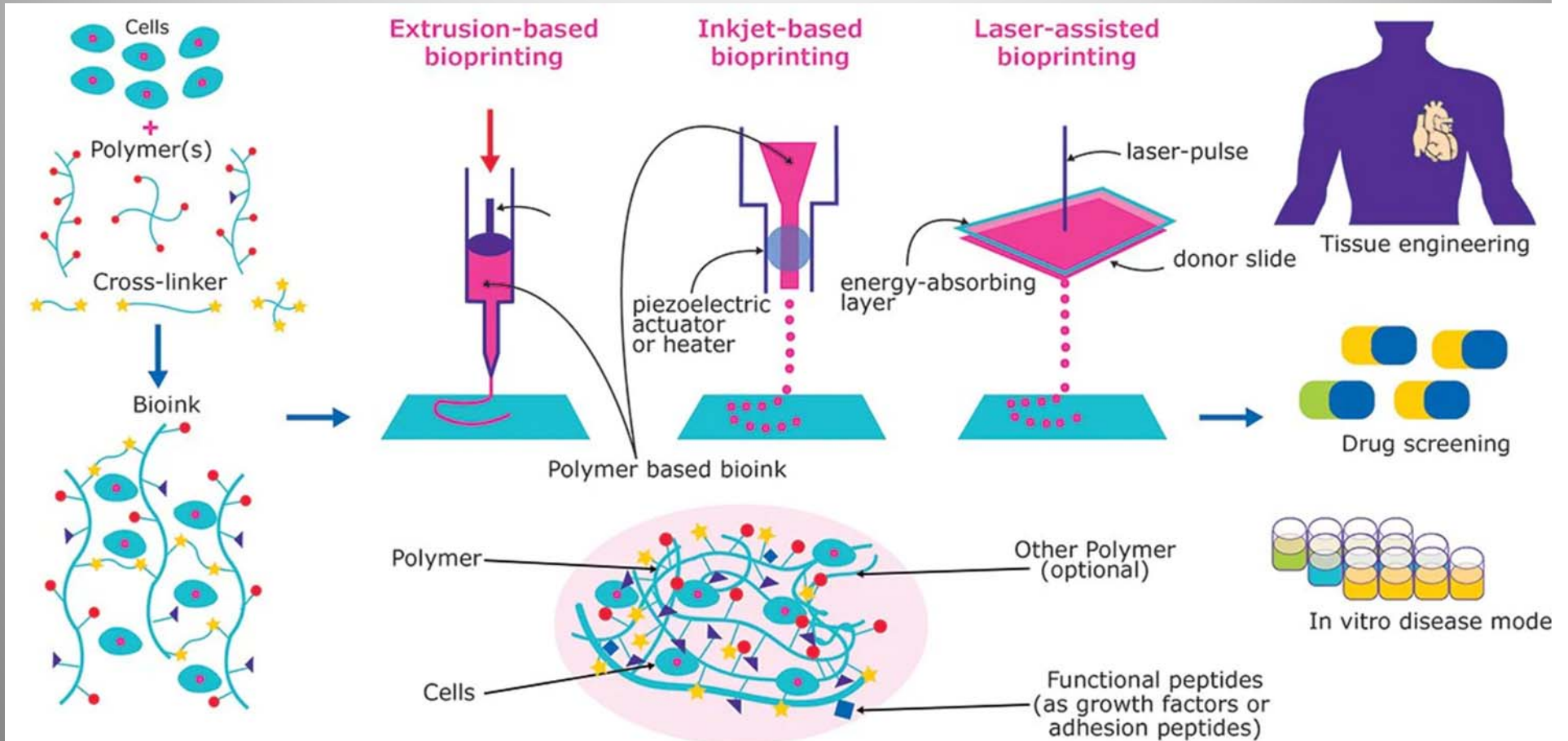


3D Bioprinting - metode

- (a) lasersko deponovanje ćelija (laser-based writing of cells)
- (b) deponovanje na bazi inkjet sistema (inkjet-based systems)
- (c) deponovanje na bazi ekstruzije (extrusion-based deposition (FDM BioExtrusion))

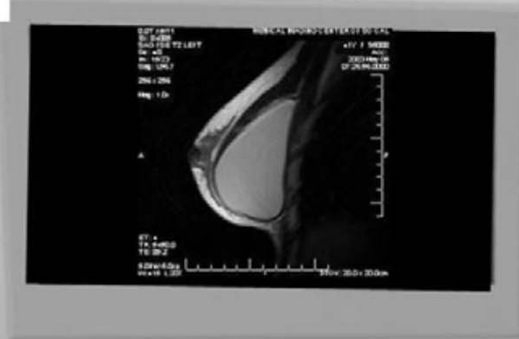


3D Bioprinting - metode



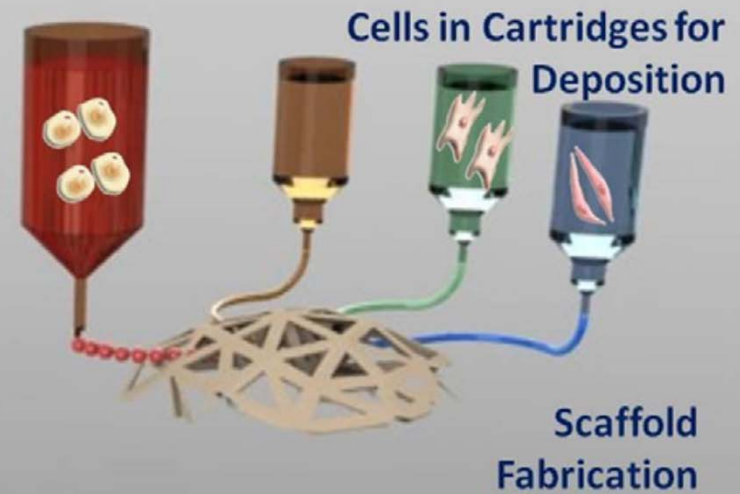
3D Bioprinting - primer

A

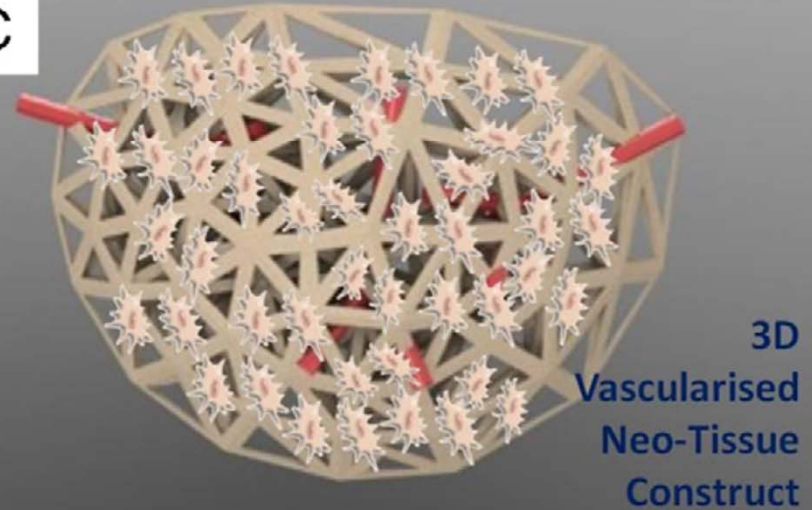


Breast MRI Image

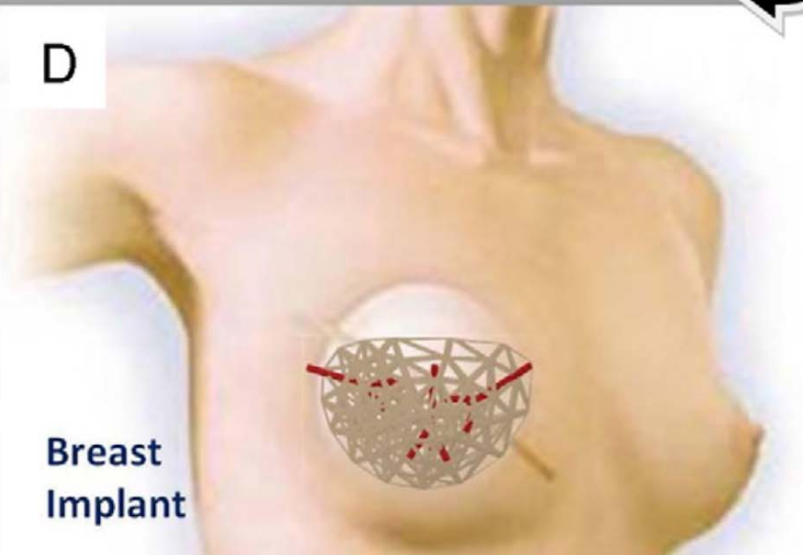
B



C



D

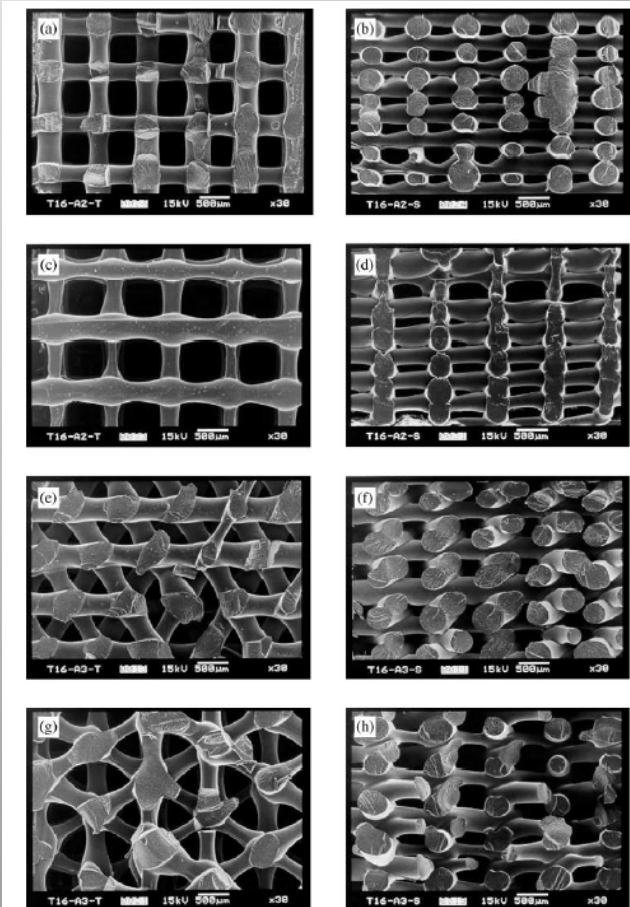
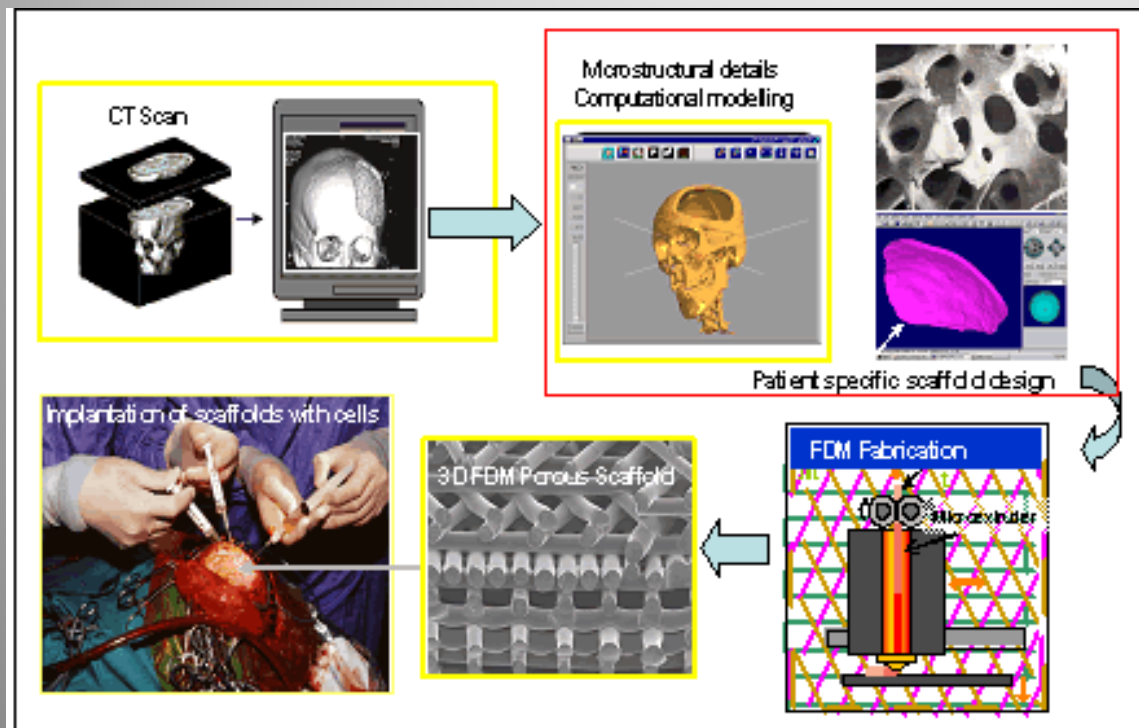


Breast Implant

FDM BioExtrusion

Biokompatibilni materijali: *Polycaprolactone (PCL)*

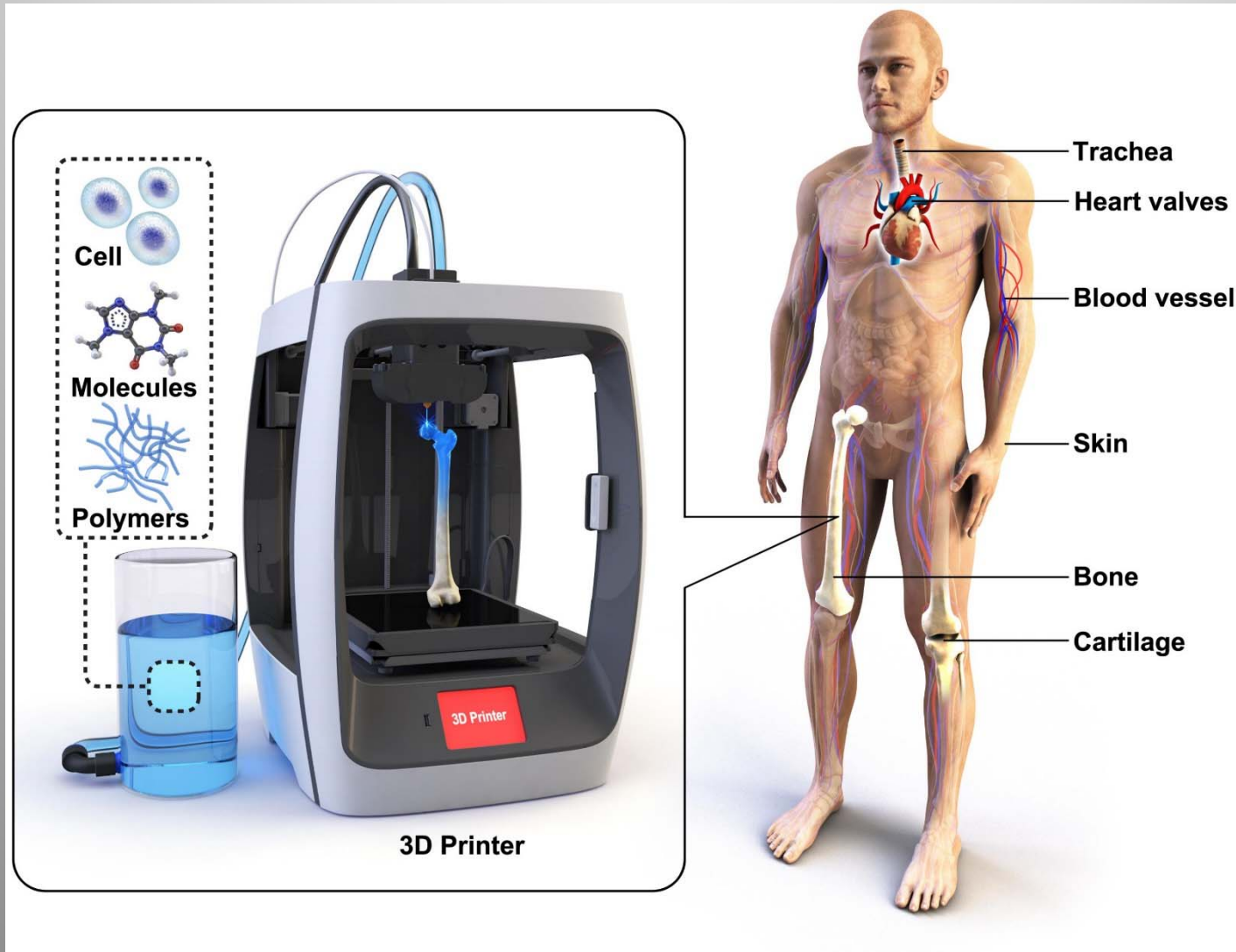
Scaffolds



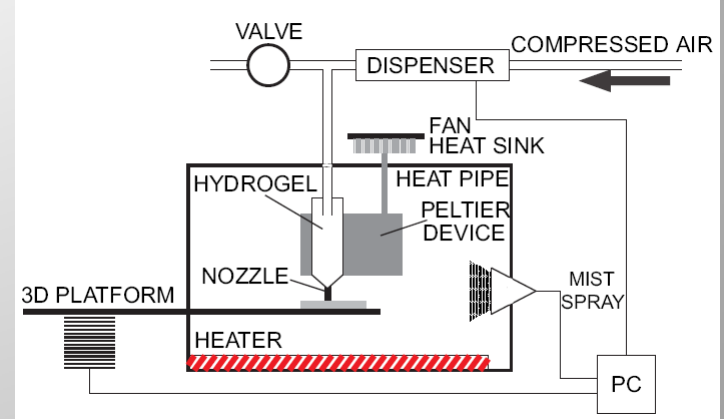
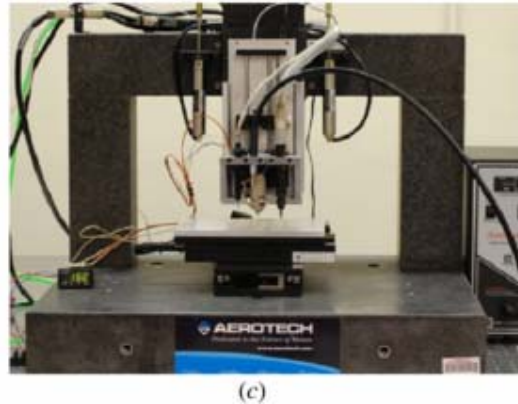
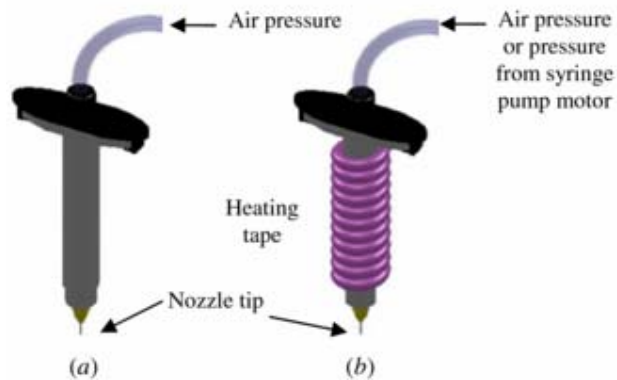
Scaffold – rešetkasta pomoćna struktura koja se koristi kao potpora u izgradnji, održavanju i popravci drugih objekata

Scaffold (medicina) - su materijali i pomoćne strukture kreirane u svrhu pokretanja željenih ćelijskih interakcija radi stvaranja novih funkcionalnih tkiva u medicini. Čelije se često „poseju“ u ove strukture i sposobne su da podrže trodimenzionalno stvaranje tkiva.

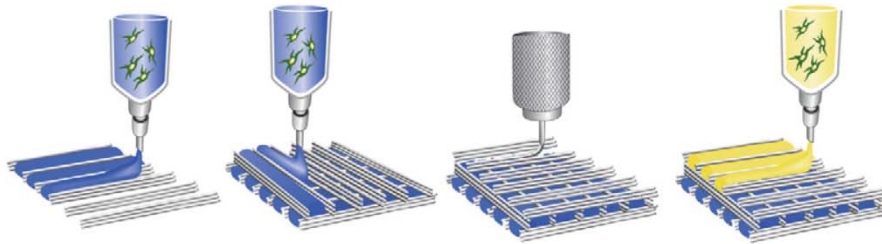
Scaffolds



FDM BioExtrusion



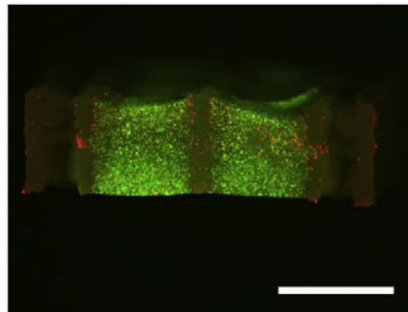
A



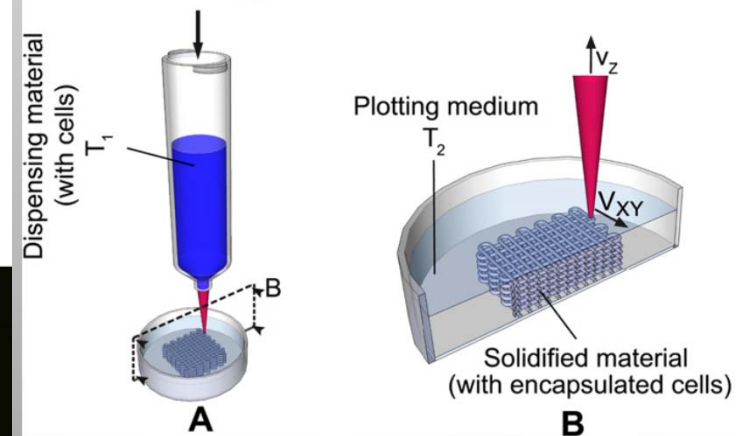
3



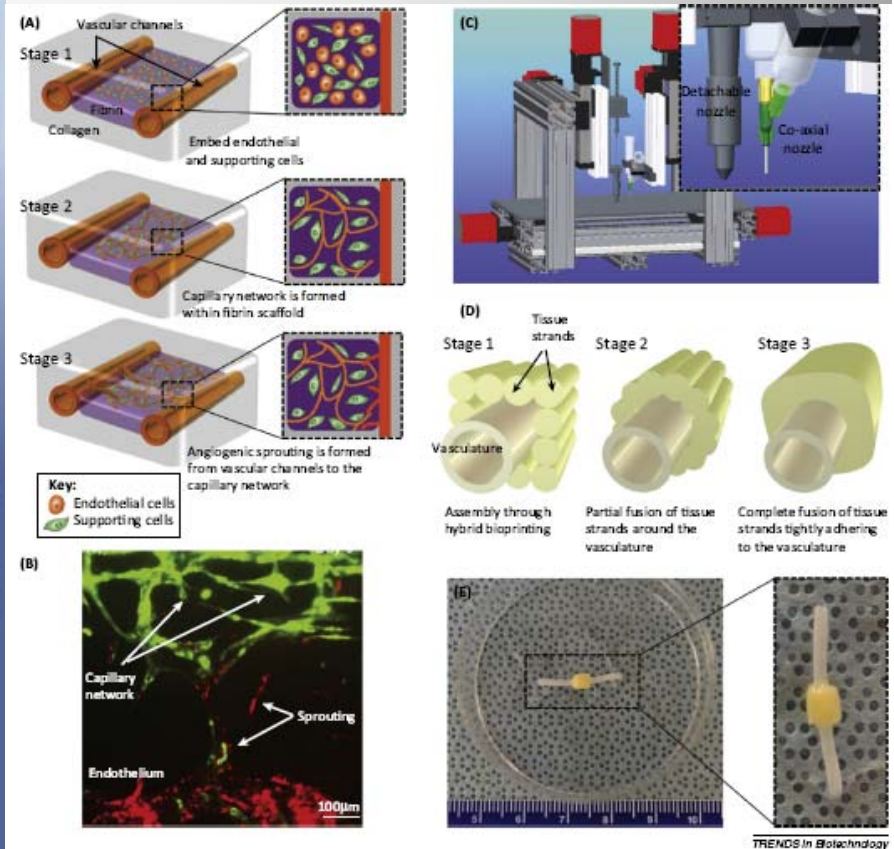
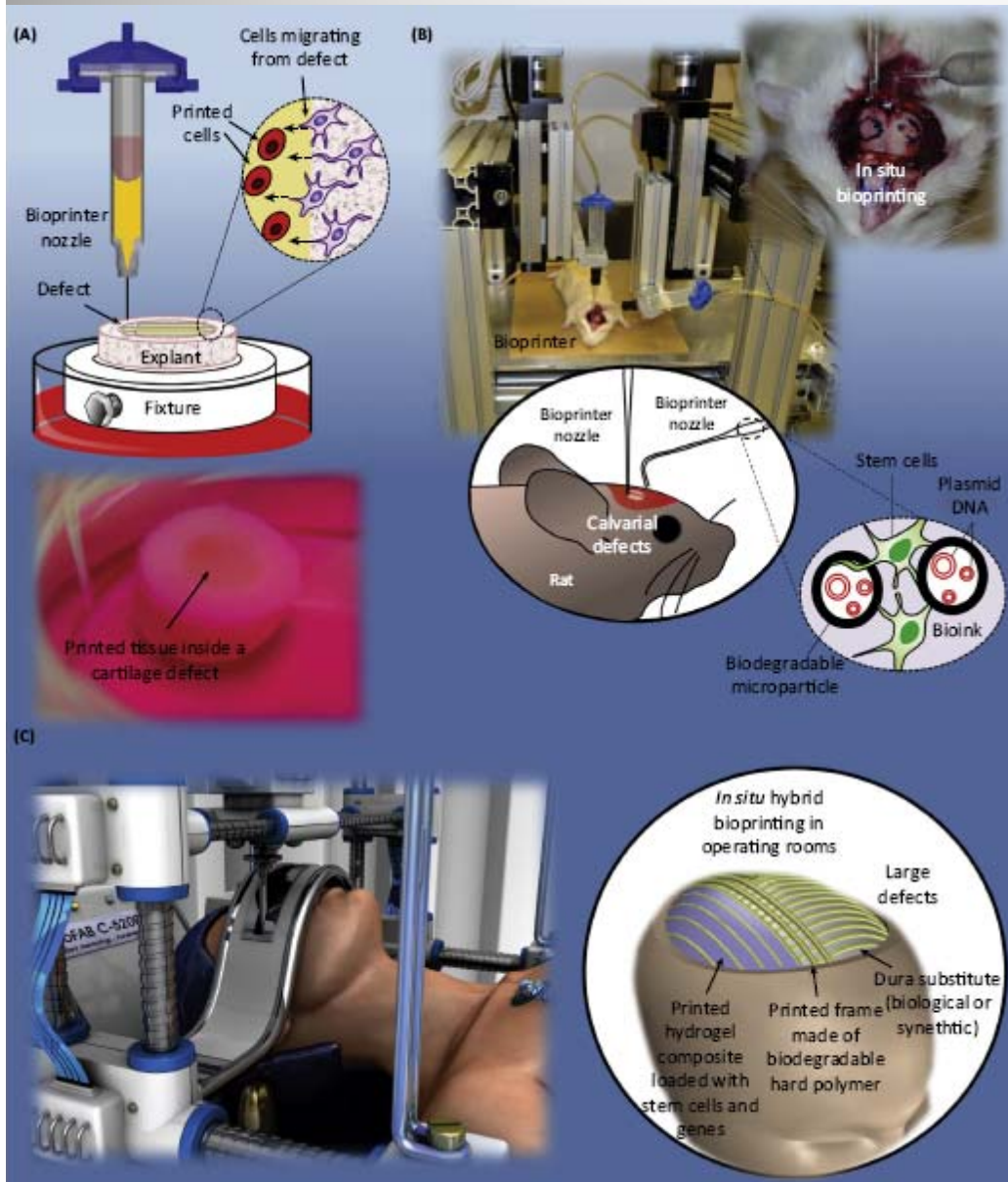
C



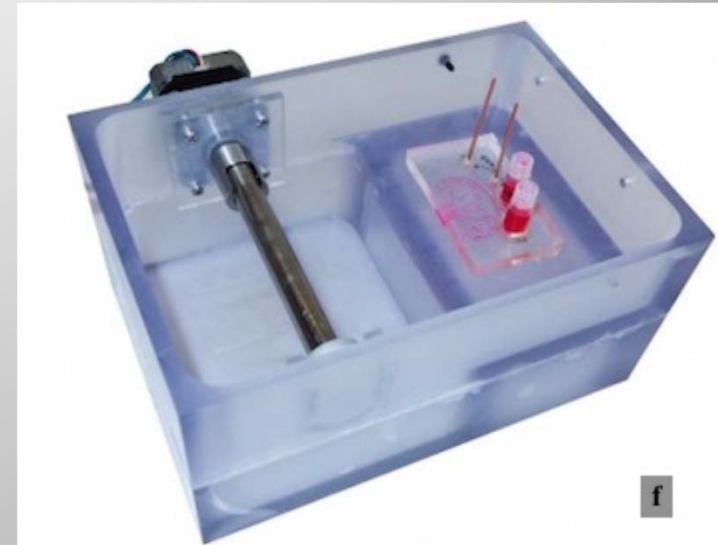
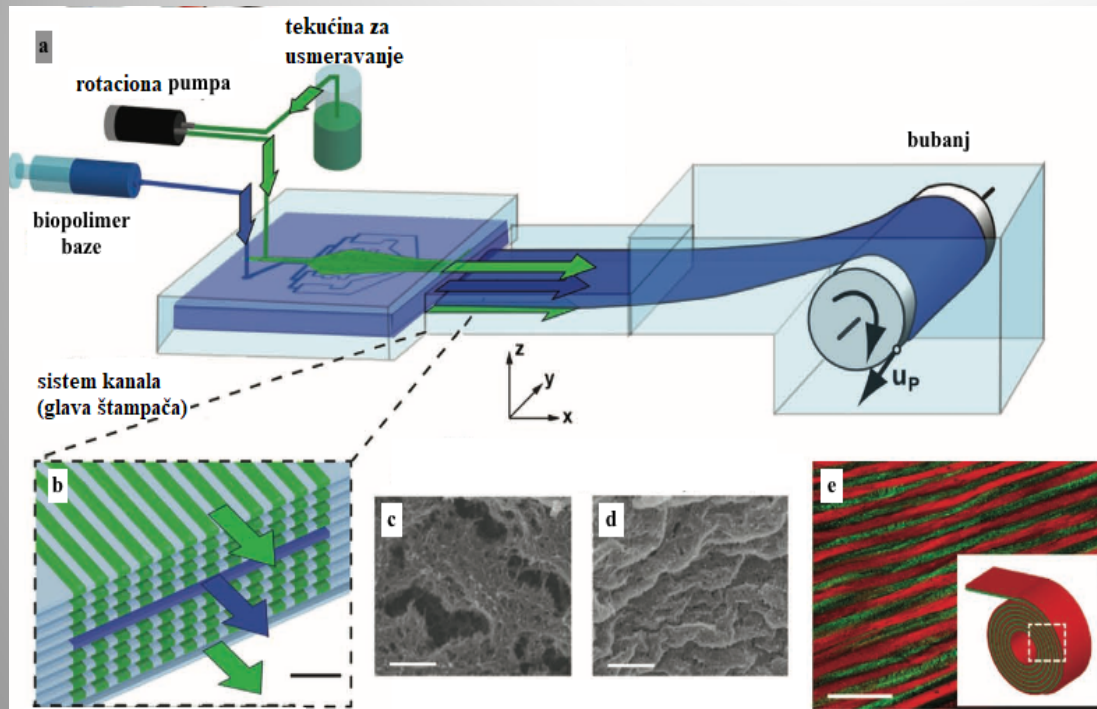
Pressure / Stepper motor



3D Bioprinting



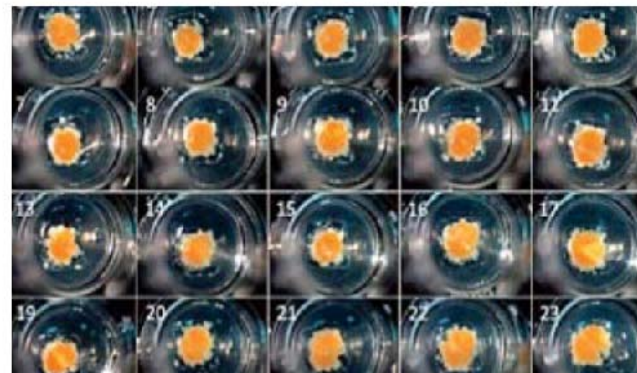
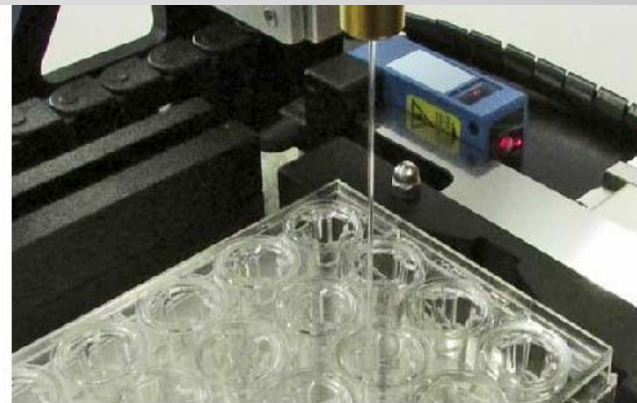
3D Biošampač



a) šematski prikaz biošampača sa smeštajem bazne (plavo) i tečnosti za usmeravanje (zeleno), potisne i rotacione pumpe; glave šampača, smer kretanja i bubnja za prikupljanje, b) smeštaj biopolimera u mozaičnom hidrogelu, c i d) uvećane fotografije pora unutar biopolimera, e) fluorescentni prikaz biopolimera smeštenog na bubnju za prikupljanje (za potrebe snimanja i prikaza u boji, u slojeve su dodane plave/zelene mikrogranule), f) fotografija biošampača

3D biošampač

- Američka kompanija Organovo pomoću bio šampača stvorila je trodimenzionalni model tkiva jetre debljine nekoliko milimetara.
- Trenutno se koristi za klinička i farmaceutska ispitivanja lekova i njihovih učinaka, znatno skraćujući vreme potrebno za njihovo puštanje na tržište.
- Osnovna razlika između klasično uzgojenog tkiva i navedenog biošampanog je njihov vek trajanja: dok klasično može preživeti nekoliko dana, biošampano tkivo može preživeti minimalno dve nedelje



3D biošampač



Evolution of Tissue Engineering and Bioprinting

- 1984** Charles Hull invented stereolithography, which enabled a tangible 3D object to be created from digital data. The technology was used to create a 3D model from a picture and enabled testing the design before investing in a larger manufacturing program.
- 1996** Dr. Gabor Forgacs (ONVD founder) and colleagues made the observation that cells stick together during embryonic development and move together in clumps with liquid-like properties, manufacturing program.
- Circa 2000** The first human patients underwent urinary bladder augmentation using a synthetic scaffold seeded with the patients' own cells (engineered, not printed).
- 2003** Thomas Boland's lab at Clemson modified an inkjet printer to accommodate and dispense cells in scaffolds.
- 2004** Dr. Forgacs developed new technology to engineer 3D tissue with only cells, no scaffolds.
- 2009** Organovo creates the NovoGen MMX Bioprinter using Forgacs technology.
- 2009-2010** Organovo prints the first human blood vessel without the use of scaffolds.
- 2011** Organovo develops multiple drug discovery platforms, 3D bioprinted disease models made from human cells.
- Today** small-scale tissues for drug discovery and toxicity testing
- Tomorrow** simple tissues for implant, (e.g. cardiac patches or segments of tubes, like blood vessels)
- Future** lobes or pieces of organs*
*For example, a patient who needs a liver transplant has lost about 80-90 % of their liver function, so a full liver is not needed to make a therapeutic impact.
- Very Future** full organs
- What Has Been Achieved So Far**
- Nerve guides - 2009
 - Blood vessel - 2010
 - Cardiac sheet or patch - 2011
 - Lung tissue - 2012

Welcome Let's begin: HOW IT WORKS

Main Components:



Creating the BioInk

1 Cells

Sourced from patient biopsies or stem cells, and grown using standard methods and techniques.



3 Collected

When enough cells are produced, they are collected to make BioInk.

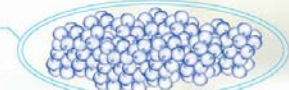
CELLS ARE THEN

- formed into spheroids or other shapes
- loaded into a cartridge to create the BioInk



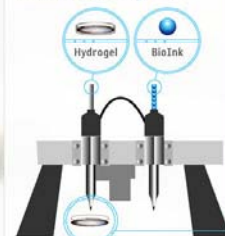
2 Cultured

Cells are cultured in a growth medium, enabling cells to multiply and grow.



Printing Process

NovoGen MMX bioprinter



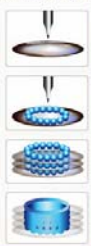
NovoGen MMX bioprinter is used to:

print a layer of hydrogel (an inert water-based gel), which functions as a space holder for the printed tissue

deposit bioink spheroids into the layer of hydrogel

Hydrogel/spheroid print process is repeated

As layers are built upon, the spheroids naturally fuse together



Maturation

Printed tissue is left in the growth medium for several weeks to grow and mature. During which time, the hydrogel is removed.



Use

Printed tissues can then be used in medical research to discover and test new drugs and investigate causes of human diseases. And, in the future, as therapies.



PRINTING A LIVER

The eventual, longterm goals for bioprinting are to produce full organs. Using today's technology, an average sized liver (1,200cc) and liver lobe (120cc) would take 10 days to print. As technology improves the speed at which human tissue and, eventually, full organs can be printed will vastly improve.



It would take 1,690,912,929,600 hours to print a liver for every member of the human race using today's processes.



3D Bioprinting

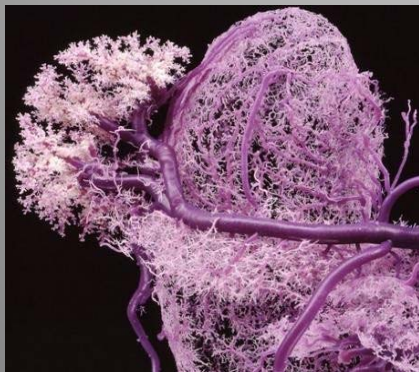
Trenutno stanje



Uho: 250 μm ćelije i kolagen iz repa pacova omogućavaju izradu ljudskog uha za 15 min. Post-procesing: 3 meseca. Služi deci sa oštećenjem sluha zbog nepravilnog oblikovanja spoljnog uha.



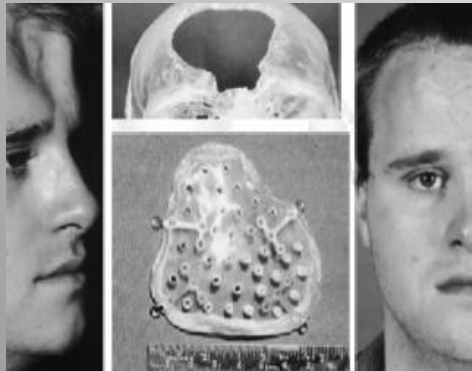
Bubreg: Gradnja sloj-po-sloj skeleta (scaffold) i deponovanje ćelija bubrega. Tkivo koje će se transplantirati pacijentu. Degradacija skeleta - in vivo.



Krvni sudovi: Čvrsti i netoksični filament na bazi šećera čine jezgro. Ćelije deponovane oko filamenata. Protok krvi rastvara šećer.



Graftovi kože: lasersko skeniranje rane za određivanje dubine i područja. Jedna mlaznica deponuje enzime, a druga ćelije. Sloj kože konačno je zatvoren ljudskim ćelijama. Korisno u ratnim i katastrofalnim zonama.

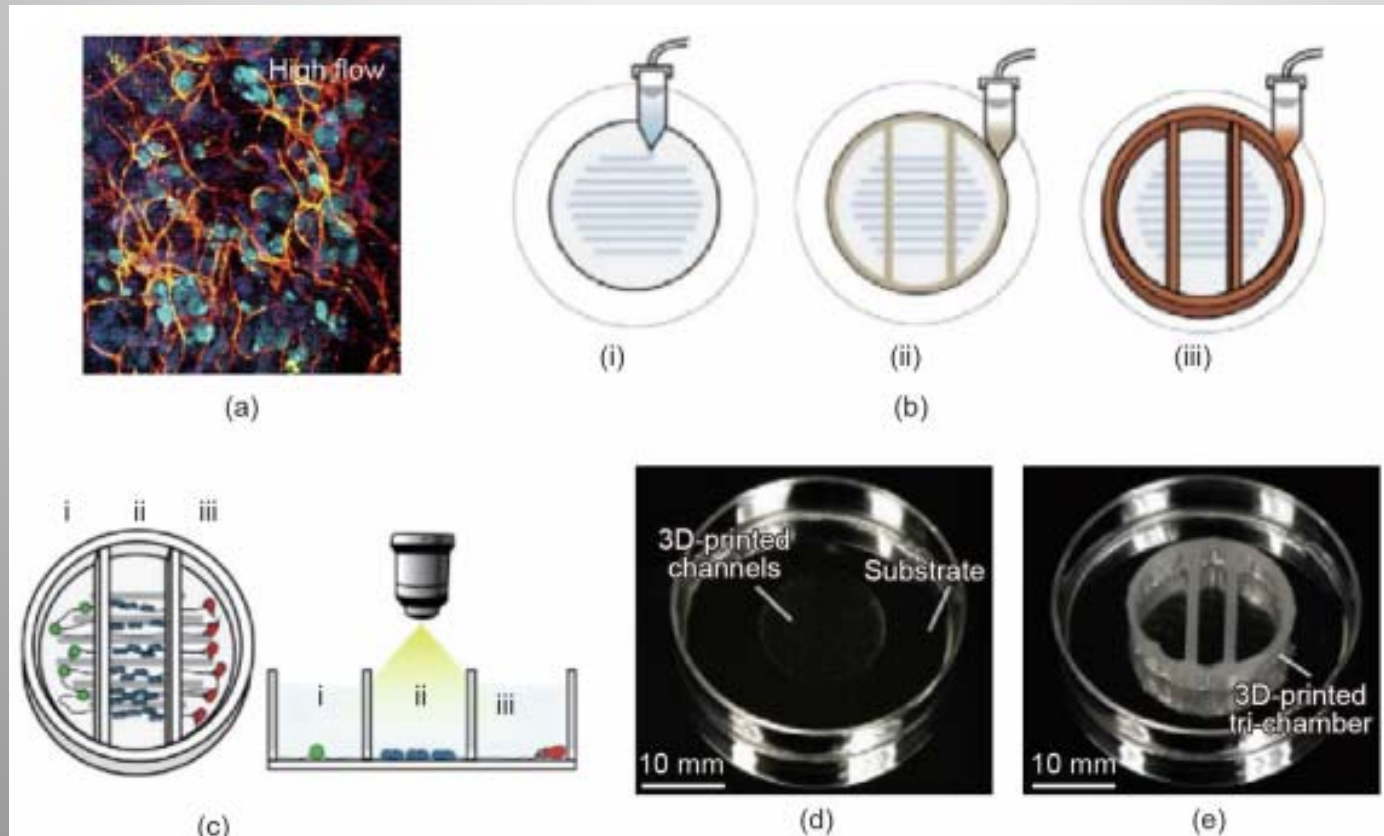


Kosti: Štampanje skeleta sa keramičkim ili titan prahom, inkubacija od 1 dana u kulturi matičnih ćelija čoveka. Primena kod složenih lomova.

\$65,000,000,000

Testiranje lekova

3D Bioprinting bubrega



(a) Developing kidney organoids cultured in vitro under high fluid flow exhibit enhanced vascularization during nephrogenesis. (b) 3D printing of a model nervous system-on-a-chip: (i) channel printing; (ii) seal printing; (iii) chamber printing. (c) Schematic of a 3D-printed nervous-system-on-a-chip with (i) peripheral nervous system neurons, (ii) Schwann cells, and (iii) terminal cell junctions. (d) Circular pattern of silicone microchannels for axonal guidance in a plastic dish. (e) Nervous-system-on-a-chip system.

Bioprinting - Prognosa

Research (today)

- Printing new Skin
- Printing cartilage & bones
- Printing replacement tissues
- Printing replacement organs

Technology Adoption (after 5- 8 years)

- Specific organ tissue replacement for important organs like heart and kidney.
- Personalized replacement for 3D printed joints with custom fit.
- Life saving 3D printed organ replacement.

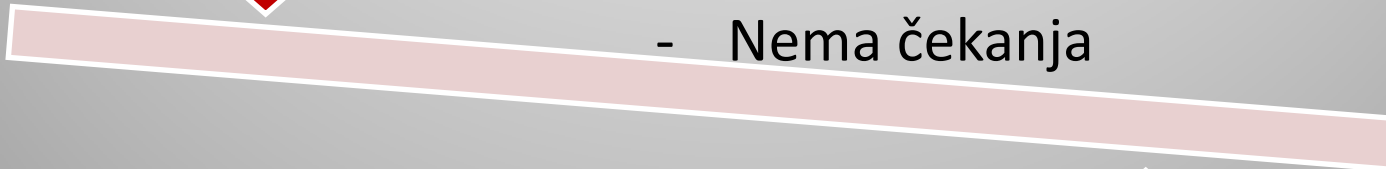
Commercialization (after 10- 15 years)

- Replacement of 3D printed organs at affordable price.
- Liver– Kidney replacement companies reach maturity.
- 3D printed replacement for all body organs available.

Za & Protiv



- Veštački organ personalizovan pomoću sopstvenih ćelija pacijenata
- Nema odbacivanja organa
- Nema potrebe za imunosupresivima koji su potrebni nakon redovne transplantacije organa
- Nema potrebe za donorima
- Nema čekanja

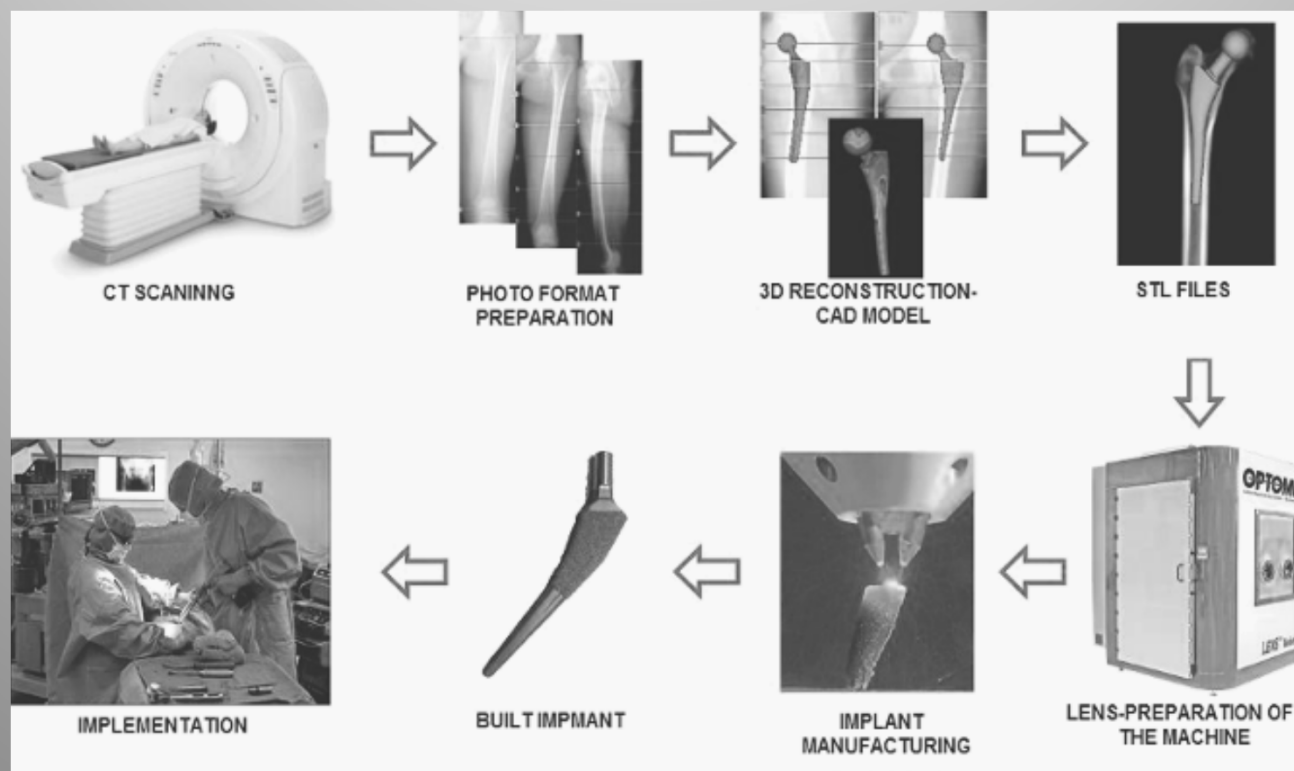


- Visoka cena Bio Printera
- Primena matičnih ćelija - kontraverze
- Cena matičnih ćelija

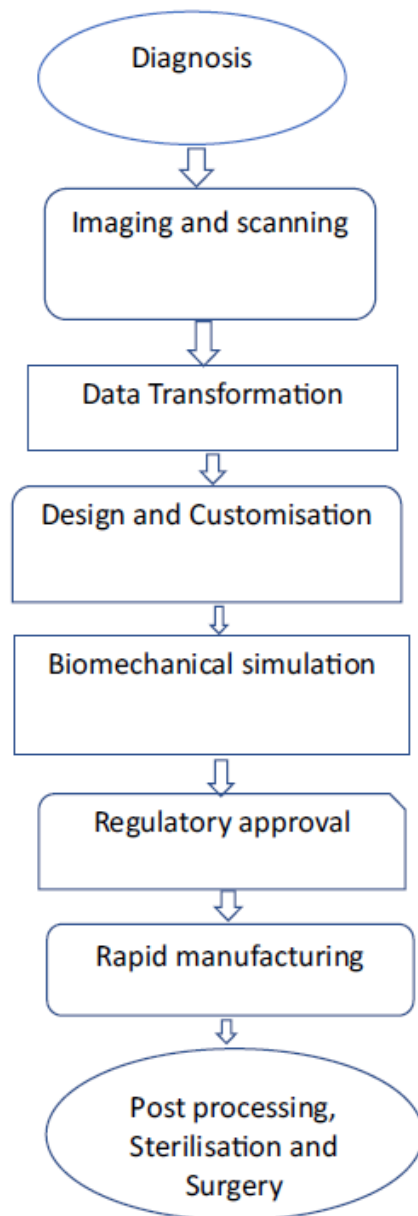


Izrada personalizovanih implantata i proteza

- Moguće je izraditi implantate i proteze bilo koje geometrije prevođenjem X-ray, MRI ili CT snimaka u digitalne .stl 3D print datoteke
- Na ovaj način, 3D štampanje uspešno se koristi u sektoru zdravstvene zaštite kako bi se napravili i standardni i složeni prilagođeni protetski udovi i hirurški implantati, ponekad u roku od 24 sata. Ovaj pristup se između ostalog koristi za izradu implantata za zube, kičmenog stuba i kuka.



Izrada personalizovanih implantata i proteza (koraci)

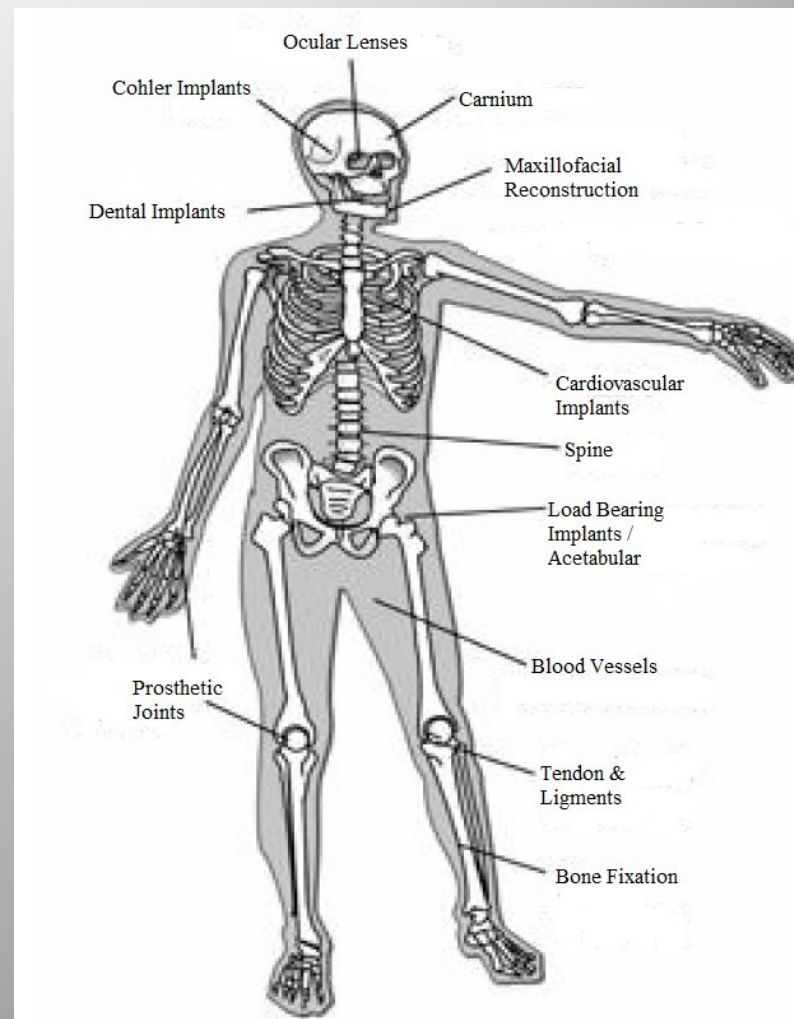


Process chain development in medical application of Additive Manufacturing.

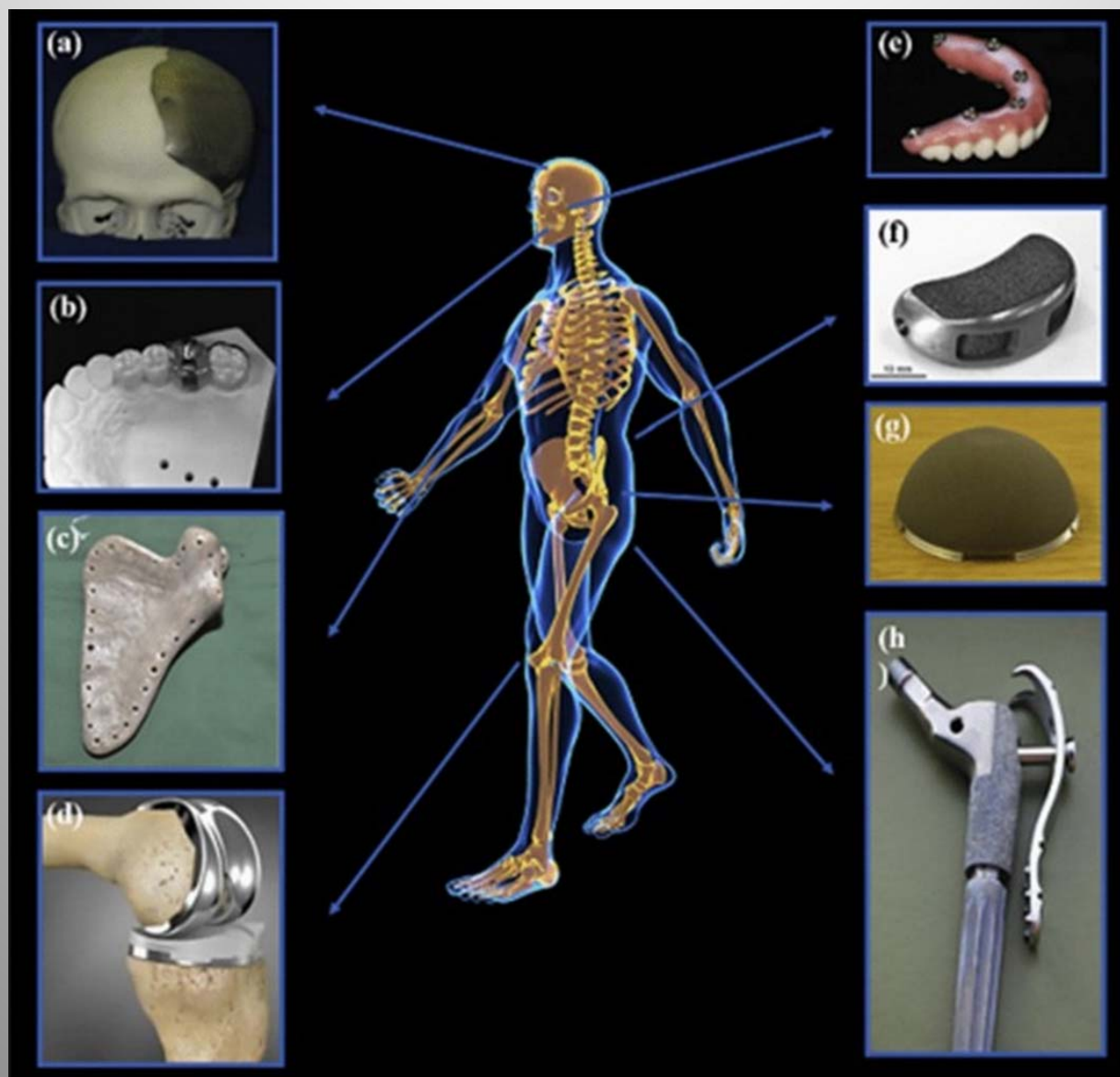
S. no.	Process chain member	Achievement	Limitation
1	Diagnosis	<ul style="list-style-type: none"> Medical diagnosis process help for deciding patient signs and symptoms for condition or diseases AM used for reverse engineering 	<ul style="list-style-type: none"> Hard for obtaining accurate and reliable data
2	Imaging and scanning	<ul style="list-style-type: none"> Medical imaging and scanning technology used for scanning and find diseases earlier Imaging and scanning used for top development from no of years These used for determining broken bone as well as diseases in human body 	<ul style="list-style-type: none"> Financial burden for the patients
3	Data transformation	<ul style="list-style-type: none"> Preparing a data from computing which derived from the original value Before statistical analysis the data transformation is necessary 	<ul style="list-style-type: none"> Need high level of skill in data analysis
4	Design and customisation	<ul style="list-style-type: none"> Medical Rapid Prototyping can design and fabricate customised implants according to required Shape and size which vary from patient to patient 	<ul style="list-style-type: none"> Need high-end designing and AM technology is costly
5	Biomechanical simulation	<ul style="list-style-type: none"> The biomechanical simulation used to improve human body parts injury They replace defective bones, skull, etc. With the help of AM technology, we achieve models, which used for adapting the user or patient needs It also contributes to analyse and describe the spines internal dynamics. 	<ul style="list-style-type: none"> Create more problem for patient if exact analysis of spine not available
6	Regulatory approval	<ul style="list-style-type: none"> Regulatory Approval is critical either of the patient or any other concern or health authorities 	<ul style="list-style-type: none"> Need authorisation whether it is feasible or not Safety and precautions are also needed
7	Rapid manufacturing	<ul style="list-style-type: none"> Medical Rapid manufacturing is used to produce medical model according to geometric accuracy in required time. 	<ul style="list-style-type: none"> Create problem if there is poor surface finish
8	Post processing, sterilisation and surgery	<ul style="list-style-type: none"> Post processing increase strength, accuracy The surface finishing of medical model and improve safety during operation It is last steps of process chain in medical. After surgery patient may feel relax as various cases discussed in different papers 	<ul style="list-style-type: none"> Increase in overall cost of medical implant

Izrada personalizovanih implantata/proteza (benefiti)

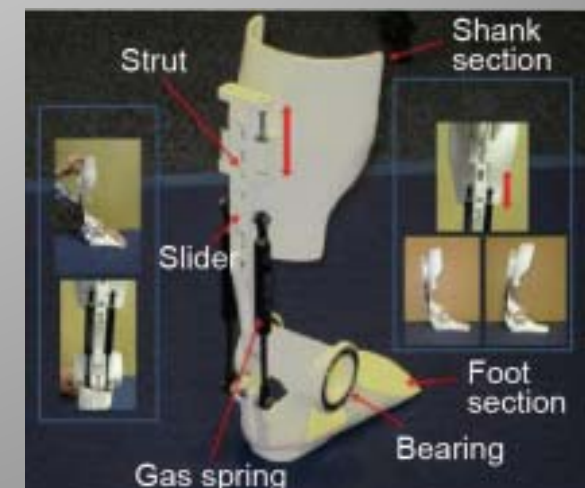
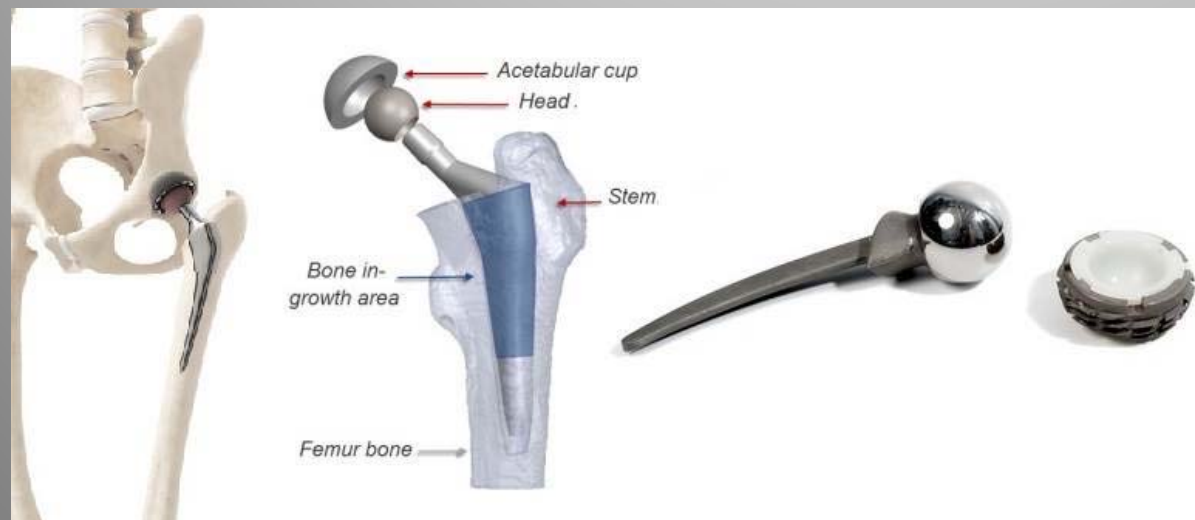
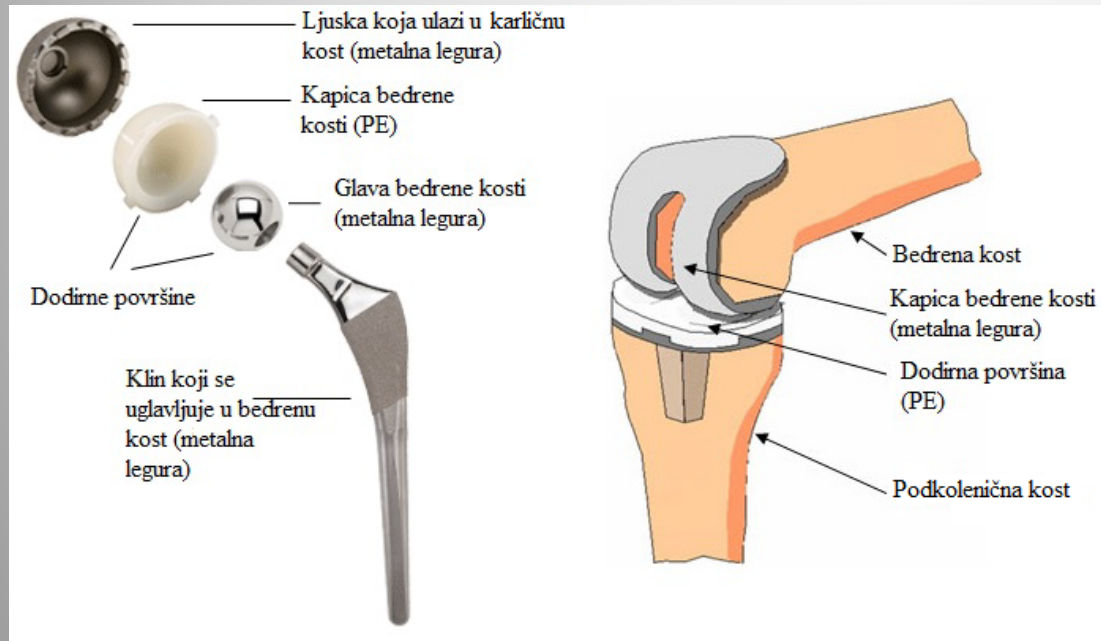
- Poboljšana čvrstoća implantata/proteza
- Dizajn i razvoj novih medicinskih implantata/proteza
- Veća tačnost implantata/proteza
- Skraćenje hiruško-ortopedskih zahvata i postoperativni tok
- Primena veštačkih kostiju
- Smanjenje težine implantata/proteza
- Bolji kvalitet implantata/proteza
- Brza izrada implantata po niskoj ceni
- Precizniji hiruški zahvati - personalizovani implantati, tačnije uklapanje na mestu traume
- Veći broj materijala. Novi materijali
- Novi pravci razvoja rekonstruktivne i estetske hirurgije



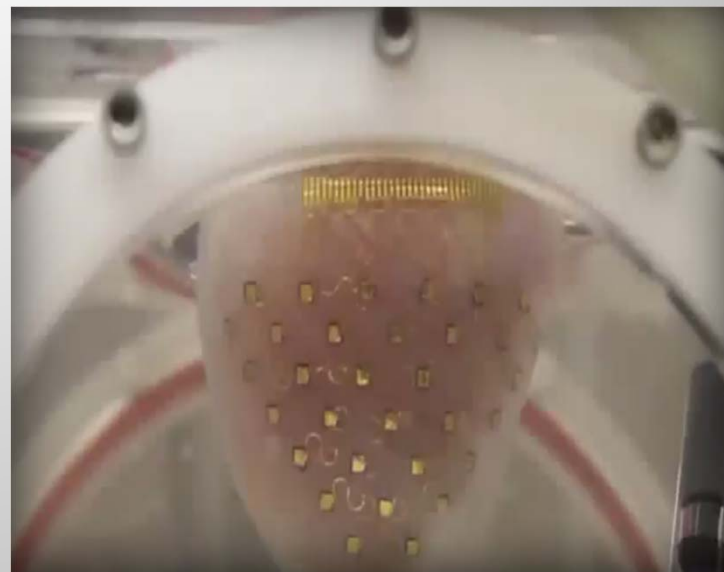
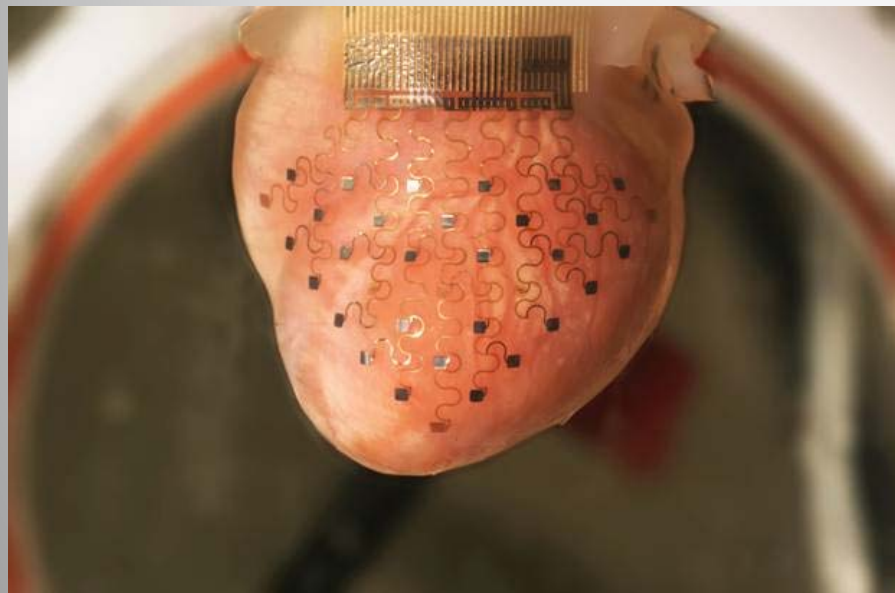
Izrada personalizovanih implantata/proteza (primeri)



Izrada personalizovanih implantata/proteza (primeri)



Izrada personalizovanih implantata/proteza (primeri – srčana membrana)



Naučnici su stvorili novu revolucionarnu elektronsku membranu koja bi mogla zameniti pejsmejkere. Obmotana oko srca omogućila je normalne otkucaje tokom vremena. Uređaj koristi „mrežno senzore i elektrode poput paukove mreže“ kako bi kontinuirano nadgledao električnu aktivnost srca i slao električne impulse za održavanje zdravog broja otkucaja srca. Istraživači su koristili tehnologiju računarskog modeliranja i 3D štampač da bi napravili prototipsku membranu i uklopili je u srce zeca, održavajući organ da savršeno funkcioniše „van tela u odgovarajućem rastvoru”.

Izrada personalizovanih implantata/proteza (primeri)



SLA implant lobanje



Titanijumski implant petne kosti

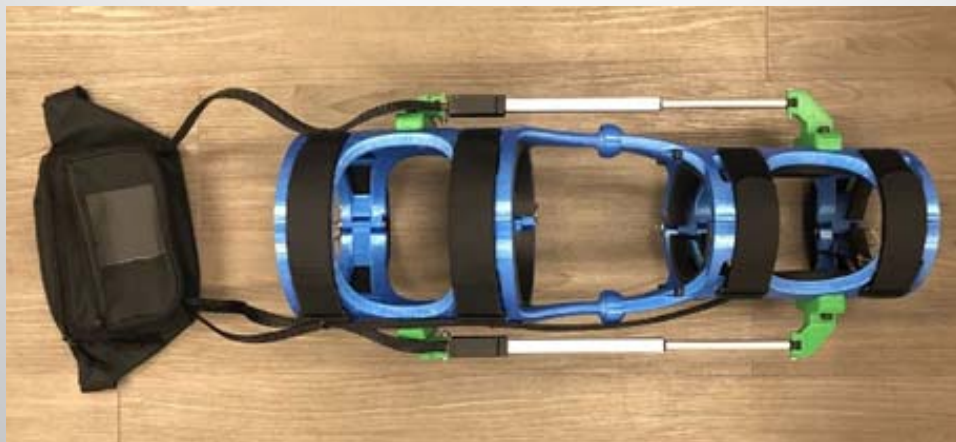


Exoskeleton dobijem pomoću FDM
omogućava paralisanoj osobi da
ponovo hoda

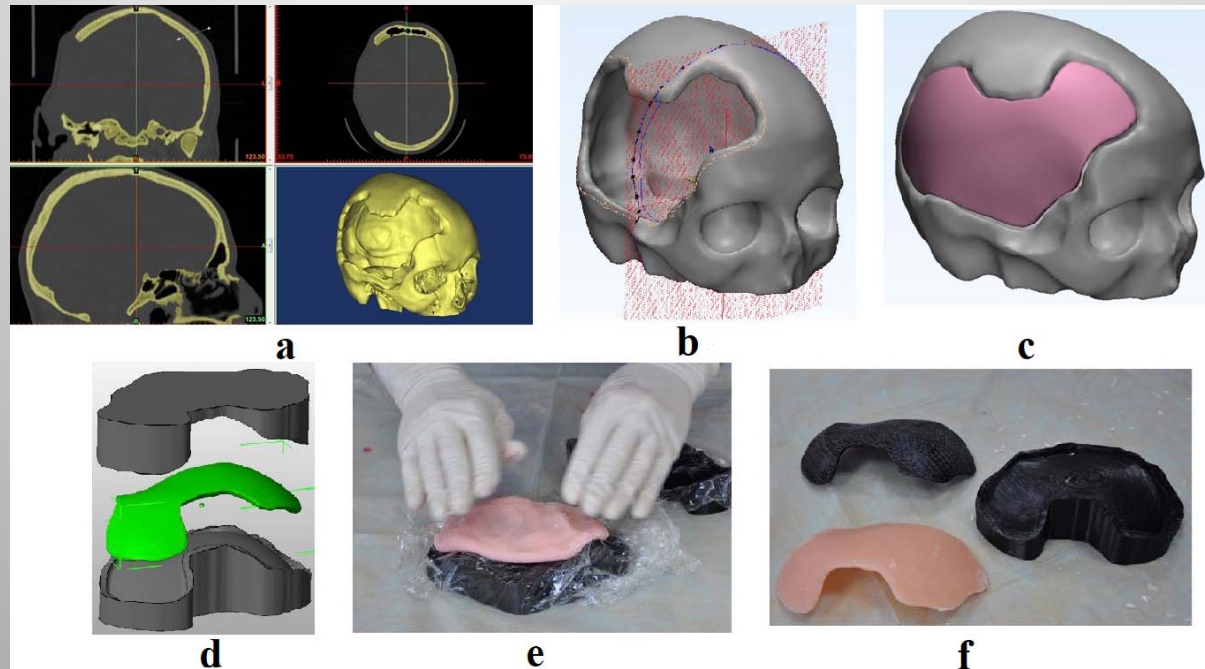


Ingestivni, samo-napajajući uređaj koji osatje u stomaku
mescima iispušta diskretne doze lekova kod pacijenata
koji zahtevaju dugotrajnu medikamentaciju

Izrada personalizovanih implantata/proteza/uređaja (primeri)



Izrada personalizovanih implantata/proteza (primeri)



Faze izrade implantata od akrilnih materijala:

a) snimke CT-a, b,c) prikaz modela lobanje s defektom i implantatom u programu za 3D prikaz, d) kalup i odlivak, e) izrada odlivka, f) gotovi deo (dole levo)

Proteza ruke dobjene 3D štampom



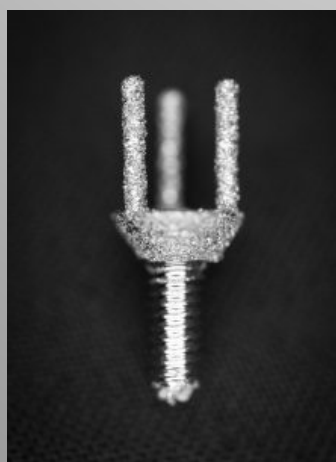
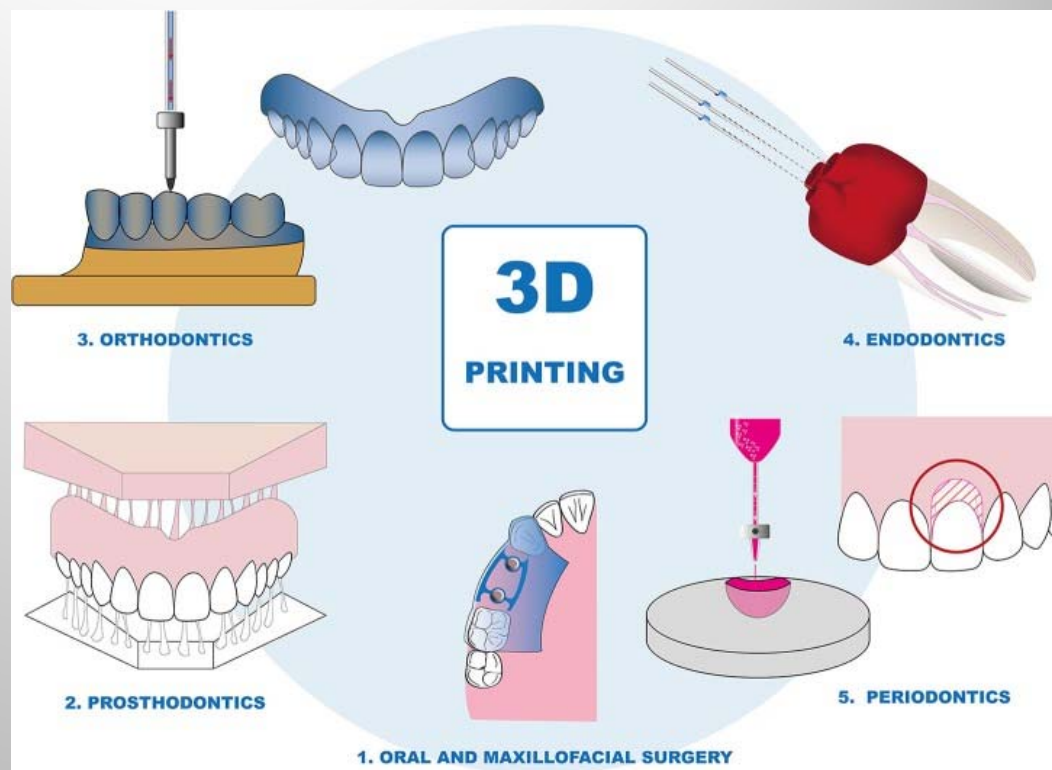
ZA BOLJI I LEPŠI ŽIVOT DEVOJČICE ROĐENE BEZ RUKE

**OVO JE VEŠTAČKA RUKA IZ 3D ŠTAMPAČA
ZA DEVOJČICU IZ VRANJA (4): Pogledajte
podvig naučnog tima sa Fakulteta
tehničkih nauka u Novom Sadu! (FOTO)**

Primena AM tehnologija u stomatologiji



Krunice zuba – SLA , PJ

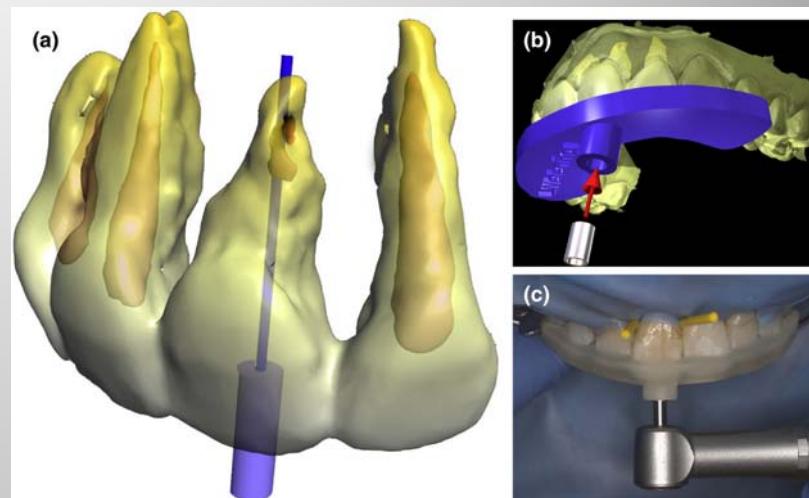
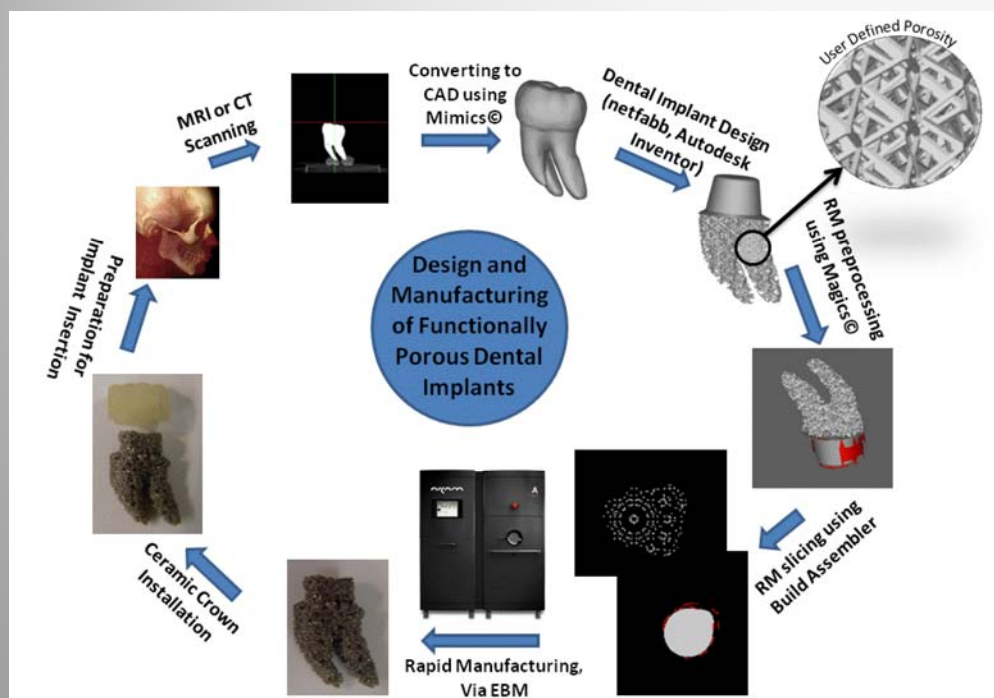


Denalni implanti - EBM



Denalni mostovi i navlake – EBM, SLM

Primena AM tehnologija u stomatologiji



Endodonski uređaji – SLA, MJ; EBM; SLM

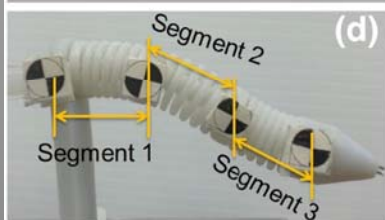
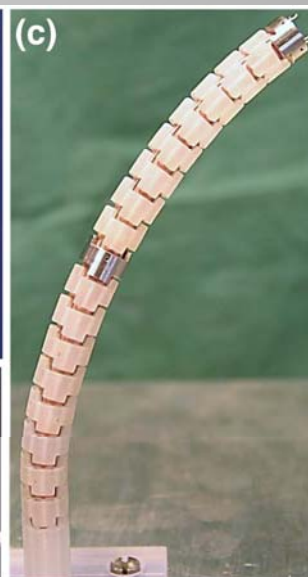
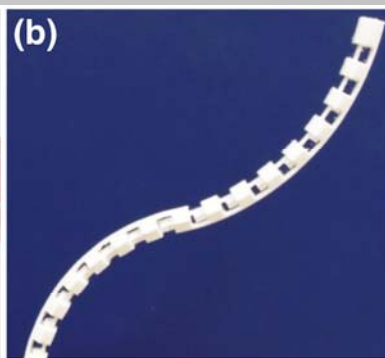
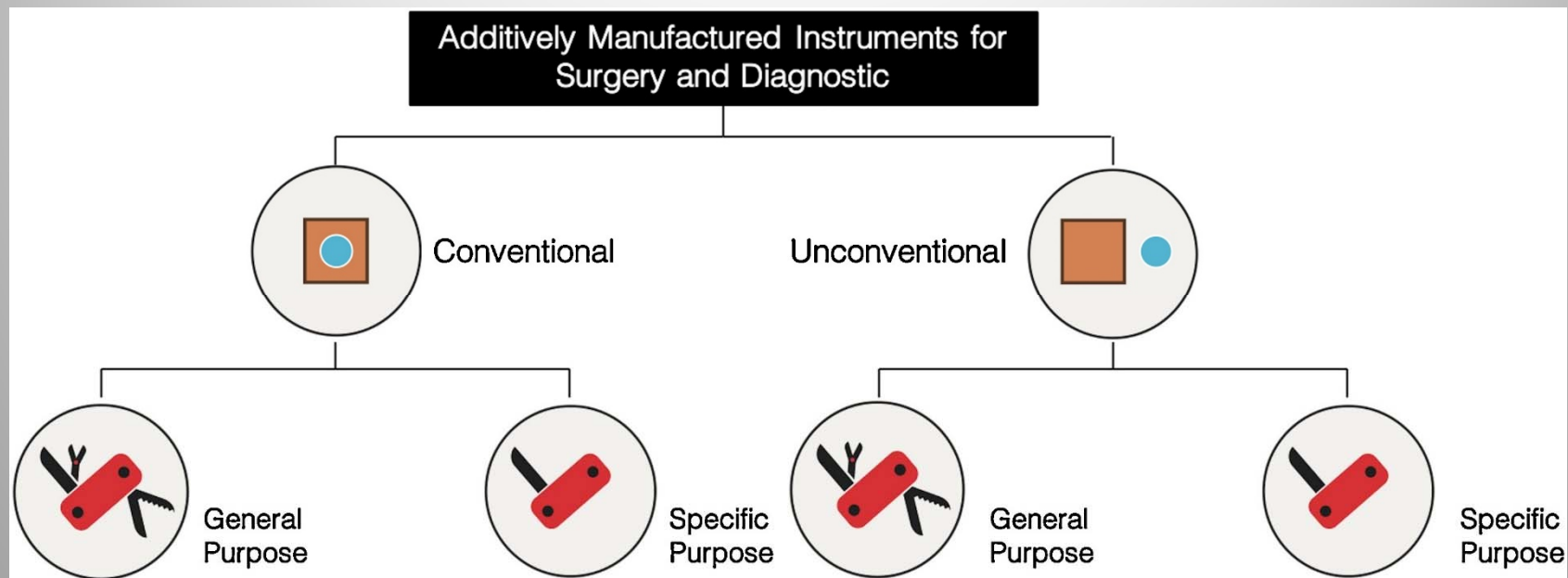


Štitnici za zube (splintovi) -SLA

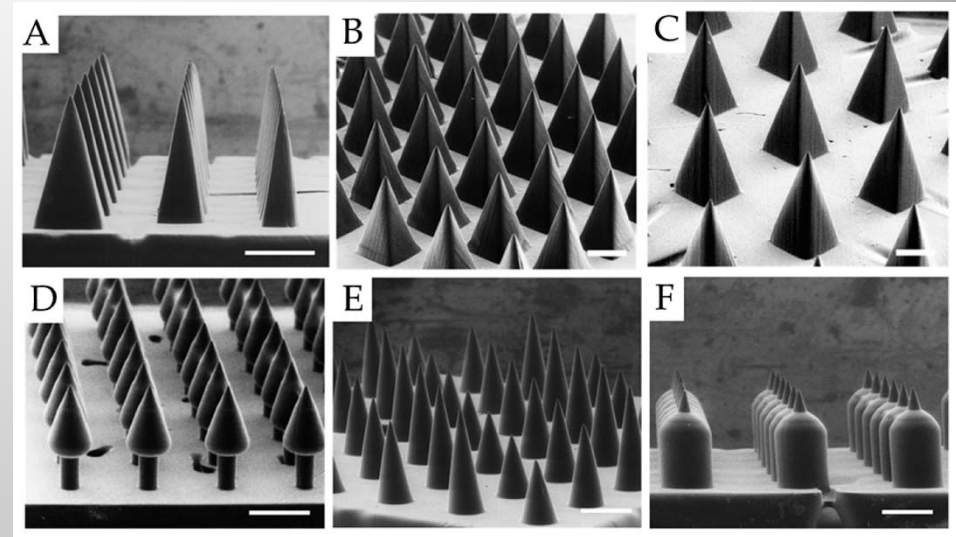


Baze parcijalnih proteza – EBM; SLM

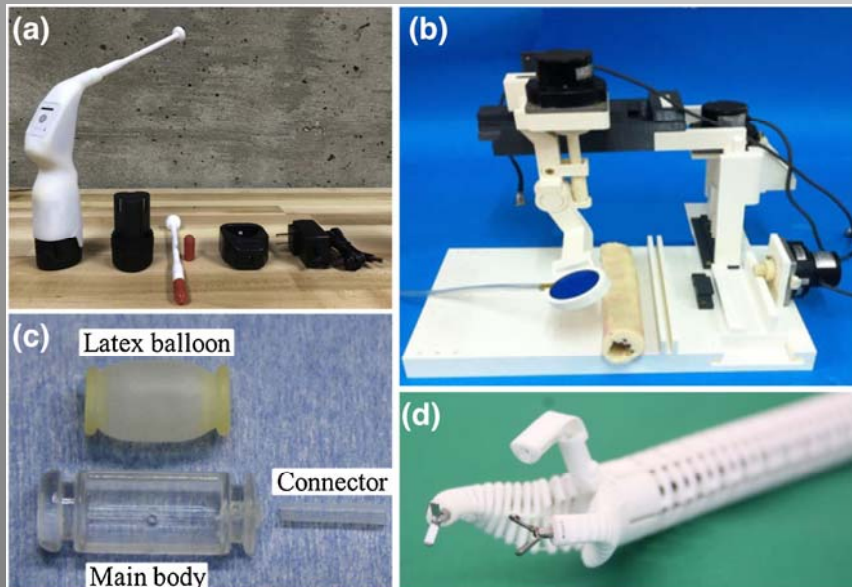
Proizvodnja hiruških instrumenata i komponenti



Proizvodnja hiruških instrumenata i komponenti



Microneedle – Mikro igle



Anatomski modeli za hiruršku pripremu

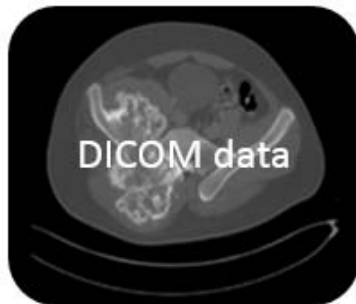
- Pojedinačne varijacije i složenosti ljudskog tela čine korišćenje 3D štampanih modela idealne za hiruršku pripremu.
- 3D štampani modeli mogu biti korisni za planiranje hirurškog zahvata.
- 3D štampani neuroanatomski modeli mogu biti naročito korisni za neurohirurge za prikaz nekih od najkomplikovanijih struktura u ljudskom telu
- Kompleksne deformacije kičmog stuba takođe se mogu bolje proučavati korišćenjem 3D modela.

Anatomski modeli za hiruršku pripremu

PATIENT COMMUNICATION MODELS

Courtesy of Maimonides Bone and Joint Center, USA

- 3D color bone model quickly and accurately created in Bespoke Modeling from CT scan
- Affordable 50% scale printed model helps patient communication and assists surgery practice sessions



"I found the 3D model invaluable in patient education, surgical planning, and physician training."
— Dr. Howard Goodman

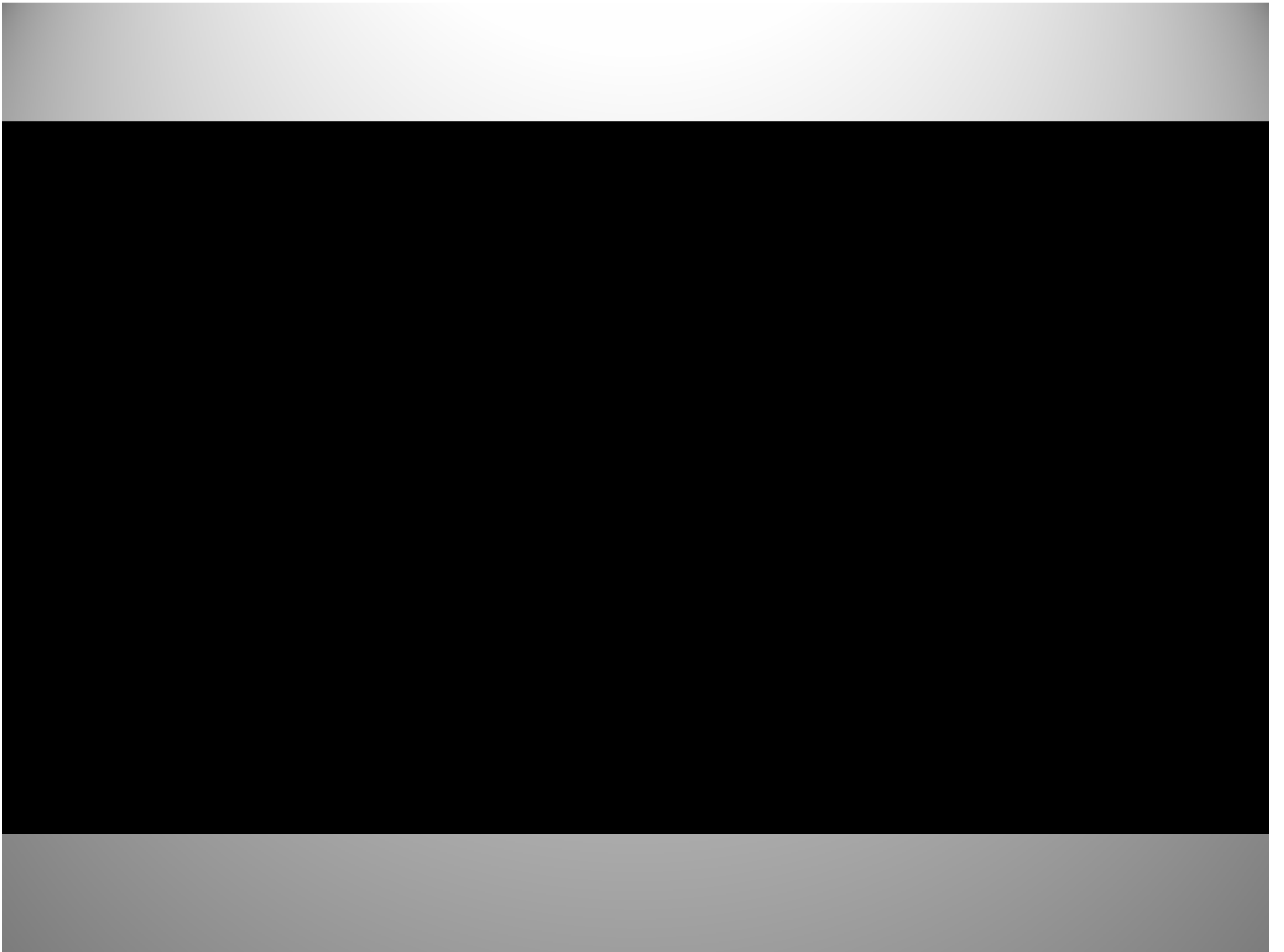
Anatomijski modeli jetre za transplataciju



Poređenje 3D štampane i stvarne jetre primatelja (levo) i donora (desno)

Edukacija i izrada medicinskih modela





Primena AM tehnologija u farmakologiji

- Tehnologije 3D štampanja se već uveliko koriste u farmaceutskim istraživanjima i proizvodnji, i donose neka revolucionarna rešenja u ovu oblast.
- Prednosti 3D štampanja uključuju preciznu kontrolu doze leka, visoku reproduktivnost i sposobnost proizvodnje razni formih dozatora sa kompleksnim profilima za otpuštanje leka
- Složeni procesi proizvodnje lekova takođe bi mogli biti standardizovani korišćenjem 3D štampanja kako bi ih učinili jednostavnijim i održivijim.
- Tehnologija 3D štampanja je veoma važna u razvoju personalizovane medicine.

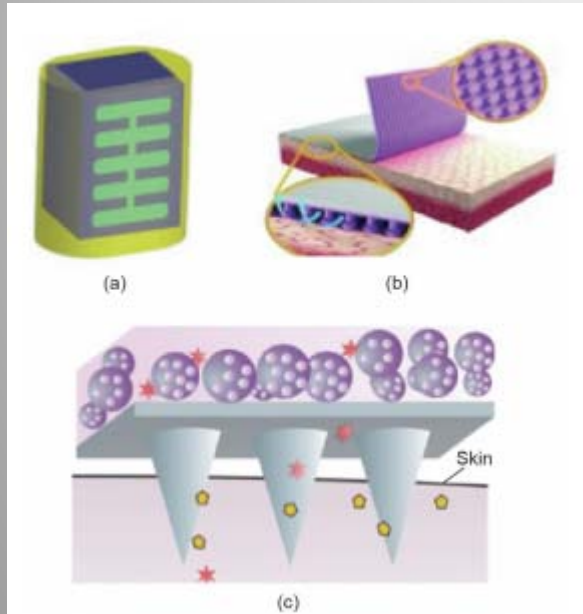
Primena AM tehnologija u farmakologiji

- Personalizovani 3D štampani lekovi mogu naročito biti korisni kod pacijenata za koje se zna da imaju farmakogenetski polimorfizam ili koji koriste lekove sa uskim terapijskim indikacijama
- Farmakolozi mogu analizirati farmakogenetski profil pacijenta, kao i druge karakteristike kao što su uzrast, rasa ili pol, da bi se odredila optimalna doza leka.
- Farmakolog tada može da pravi (štampa) i distribuira personalizirane lekove putem automatizovanog 3D sistema za štampanje.
- Ako je potrebno, doza se može dalje prilagoditi na osnovu kliničkog odgovora.

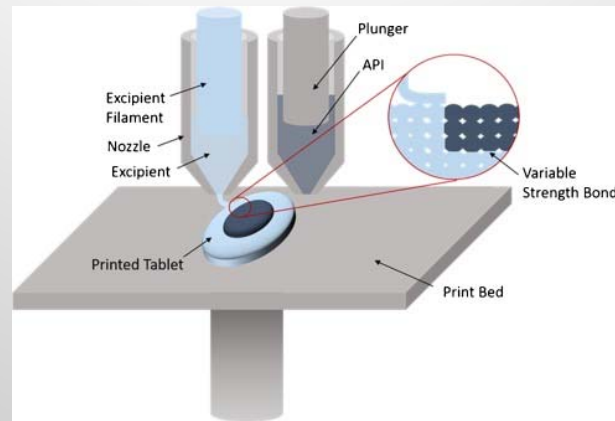
Primena AM tehnologija u farmakologiji

- Primarne tehnologije 3D štampanja koje se koriste za farmaceutske proizvodnju su **inkjet based** i **inkjet powder based** 3D printing tehnologije.
- Pri proizvodnji lekova na bazi inkjet tehnologije, inkjet štampači se koriste za brizganje komponenti leka i vezivnog sredstva u obliku malih kapljica preciznim brzinama, putanjama i dozama na podlogu. Najčešće korišćeni supstrati uključuju različite vrste celuloznog, premazanog ili nepremazanog papira, mikroporozne biokeramike, staklenih skeleta (scaffolds), metalnih legura i filmova na bazi skroba.
- U 3D štampanju na bazi praha, glava inkjet štampača nanosi "mastilo" na osnovu (bazu) od praha. Kada "mastilo" natopi prah, on ojačava i stvara čvrsti doznani oblik, sloj po sloju. "Mastilo" može uključivati aktivne sastojke, kao i vezivno sredstvo i druge neaktivne sastojke. Nakon što je 3D štampani oblik osušen, čvrsti objekt se uklanja iz podloge praha.

Primena AM tehnologija u farmakologiji



- (a) Tablets of oral medicines.
- (b) Patches of transdermal drugs
- (c) Microneedles of transdermal drugs



Phase	Image
3D printed pellets containing paracetamol and ibuprofen	
Six layered polypill in cylindrical and ring-shape formations	
3D printed tablets of cylindrical and novel geometric lattice shapes	
Novel anti-counterfeit measure using QR codes and smart material inks	

Primena AM tehnologija u medicini/stomatologiji

(sumarni pregled)

Summary of the main characteristics, advantages and limitations, and challenges and future directions of AM technologies in clinical applications of pharmaceuticals, medical implants, and medical devices.

Clinical application	Main characteristics	Advantages	Limitations	Challenges and future directions
Oral drug	Produce oral drug with complicated structures and elaborate shapes	Incorporation of drug-loaded formulations or APIs; dose accuracy, convenience, and time-effectiveness	Technical and quality control limitations	Digital health
Transdermal drug	Exquisite precision has been leveraged for the manufacturing of automatically adaptable patches	High thermal stability, drug-loading capacity, and resolution; manipulation of the release kinetics of drugs	Technical and quality control limitations	Digital health
Hard-structure implants	Allow accurate control of the internal pore structure of porous architectures, and allow complex geometries to be manufactured with repeatability	Versatility, high precision, accuracy, surface finish, and structural integrity; suited for creating highly porous implants; durable	Implant failure	Enhance biocompatibility and function
Soft-structure implants	Recreating human structures within cell-compatible materials	Dramatically improved functions of the cells of organs	Major issues with the long-term viability of the cells and cell proliferation control	Toward finer and more complex structures
Diagnostic tools	Visualization of patient-specific organ anatomy	The amount of information has been dramatically increased by preoperative planning beyond the features of individual organs	Long printing time	Shorten printing time; improve the accuracy of diagnosis
Prostheses	Designed to achieve high strength-to-weight ratios	Require less material to achieve similar performance capabilities, potentially resource efficient	Functions and mobility	Long-term limb replacement
Orthoses	Fabricating custom foot orthoses, ankle-foot orthoses, and wrist splints	Good fit and adequate strength	A lack of clinical and design interface; uneconomic throughput and material cost; limited material strength	Durability and safety of orthoses
Surgical tools	Designing and fabricating patient-specific, customized surgical instruments	Allow for a more controlled and simplified operative experience; reduce the cost of tools	Modest performance	Improve performance by technological innovation

