Significance of Substratum for Bioprinting: A Review

Subramanian Gunasekaran, PhD, President, Encoll Corp. 4576 Enterprise St, Fremont, CA 94538, USA.

Introduction:

3D bioprinting uses three dimensional printing techniques to intermix cells, growth factors, and/or biomaterials to fabricate medical devices, often with the intention of imitating natural tissue characteristics¹. Normally this process is made by layering biomaterials one over the other. The purpose of this article is to compare the relative efficacies of different biomaterials used for this process. The word Bioprinting refers to the inoculation of viable cells (primarily stem cells) and printing this Bio-Ink over a gel-like biomaterial to mimic the extracellular matrix environment, supporting cell adhesion, proliferation, and differentiation after printing. Accordingly, Bio-inks must have the following characteristics²:

- Print temperatures that do not exceed physiological temperatures
- The matrix should be compatible for cell growth & development
- Bioactive components that are non-toxic and able to be modified by the cells after printing

Methods:

A considerable amount of literature study was accomplished to fulfill the required methodology for this review article. Accordingly, we have focused on varied scientific publications about the biocompatibility of different matrices and their tissue regenerative capabilities. For relative comparison purposes, we have taken into consideration all kinds of hydrogels that are used to prepare bioprint/bio-ink matrices. Such materials include natural polymers like collagen, hyaluronic acid, chitosan, heparin, alginate, fibrin, and synthetic materials like polyvinyl alcohol, polyethylene glycol, sodium polyacrylate, acrylate polymers, copolymers³. We also try to compare the interaction between the cell receptors of the cultured cells and the hydrogel matrix may not be compatible for proper function of the cell^{4,5}. The outcome of this review is to help bring about significant changes in the field of Bioprinting for improving this field of research.

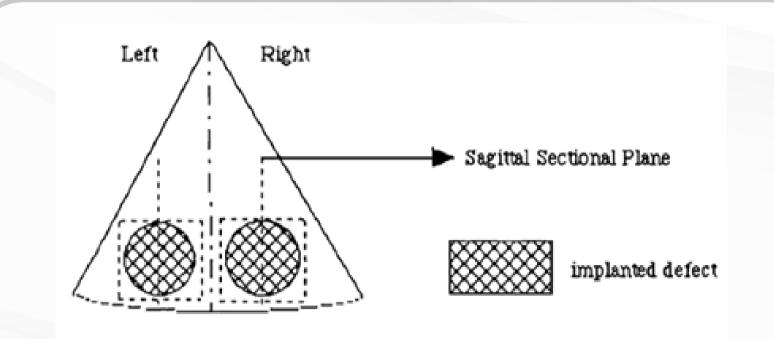


Fig 1. Diagrammatic representation of rabbit skull defect analysis

OUTCOME OF THE STUDY	
Complete osseous healing response in the defect site	
Very little, if any, new bone has been formed. Mostly filled in with a fibrous tissue	
No new bone growth within 4 weeks post implantation	
No new bone nor a dense fibrous tissue ingrowth	

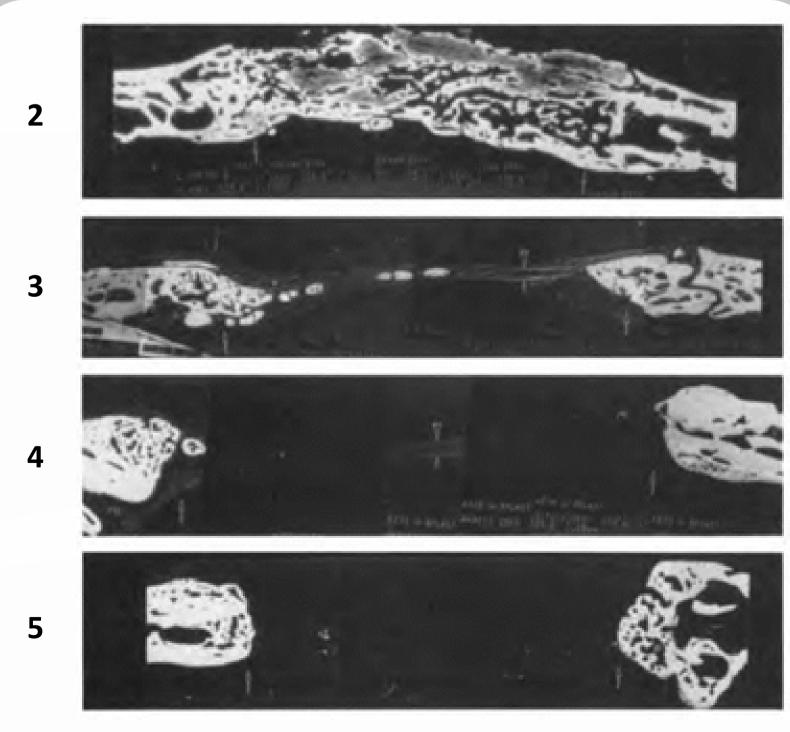


Fig 2. Relative Biological Efficacy of Different Matrices

Results:

The most important result of our analysis discourages the most popular usage of carbomer gels made of Acrylate/Polyacrylate. Even though it absorbs high amount of water⁶ (9:1 w/w), the receptors on the cell membrane do not find a comfortable environment to function normally when surrounded by a synthetic polymeric matrix.

Discussions:

Moving on to compare the other synthetic matrices, the finding remains the same. With the respect to the other natural molecules, none of them seems to be efficacious compared to the purified Type-I Collagen as a matrix. This can be further evidenced through an animal experiment that compares the relative efficacy of biomaterials in delivering growth factors to foster bone formation. It has been proven that mineralized collagen seems to possess the chemical and structural resemblance with native bone. As a result, only the mineralized Type-I collagen leads to ultimate healing of the osseous defect equivalent to that of the autologous bone graft⁷. Only this material seems to suit the best to mimic the biological milieu needed to bridge the gap by enhancing the affinity of the cell to the matrix ^{8,9}.

References:

- 1. https://en.wikipedia.org/wiki/3D_bioprinting
- 2. https://biomaterialsres.biomedcentral.com/articles/10.1186/s40824-018-0122-1
- 3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6439477/
- 4. https://encyclopedia.pub/entry/21456
- 5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5883979/
- 6. https://journals.sagepub.com/doi/pdf/10.3109/10915818209013151
- 7. https://www.taylorfrancis.com/chapters/edit/10.1201/9780203751367-13/comparative-utility-mineralized-collagen -osteoinductive-material-subramanian-gunasekaran-ian-bathurst-brent-constantz-james-quiaoit-john-ross-philip-barr -denis-gospodarowicz
- 8. https://www.intechopen.com/chapters/80857
- 9. https://link.springer.com/article/10.1134/S1990519X21050059