Composite Bioinks That Can be Injected or 3D Bioprinted to Aid Osteochondral Defect Repair

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Golden Jubilee Foundation
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Background

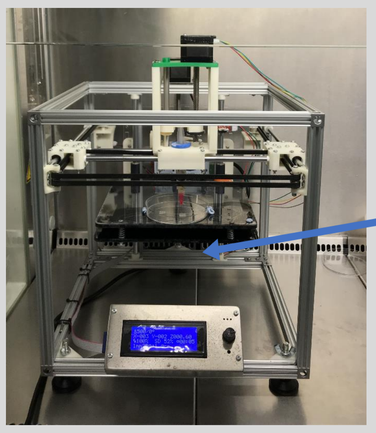
Despite having a highly specialised function and structure, articular cartilage (AC) has poor intrinsic capacity for healing and repair. Current AC repair techniques have limitations and demand for joint replacement surgery is increasing exponentially. However, by combining cells, biomaterials and techniques such bioprinting, 3D biofabrication offers a novel approach to help tackle AC defects.

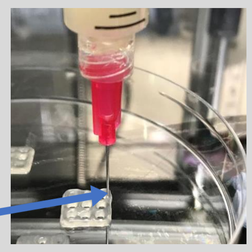
Aim

Apply a biofabrication approach to support osteochondral repair.

Methods & Results

A custom bioink was developed by mixing different ratios of methacrylted alginate (AlgMA) and gelatin (GelMA). This allowed development of a bioink that could be reliably 3D bioprinted down to 100 micrometre resolution whilst more substantial constructs could also be produced.

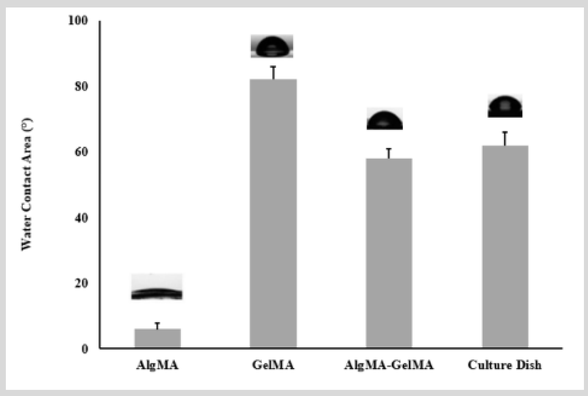




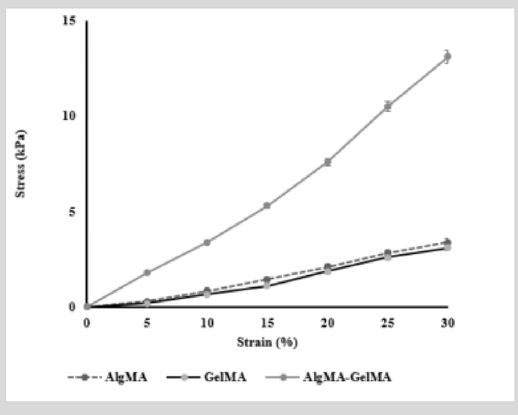
Bioprinted scaffold

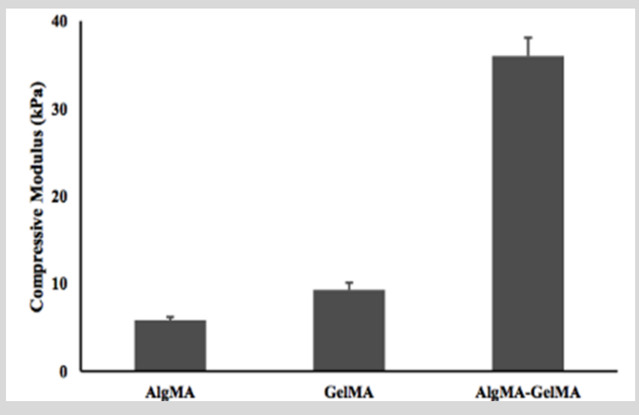
100µm thick

Measuring the hydrophilic properties of the composite bioink, it was apparent that AlgMA/GelMA blends had optimised cell culture performance, with hydrophilic culture properties similar to a cell culture dish.



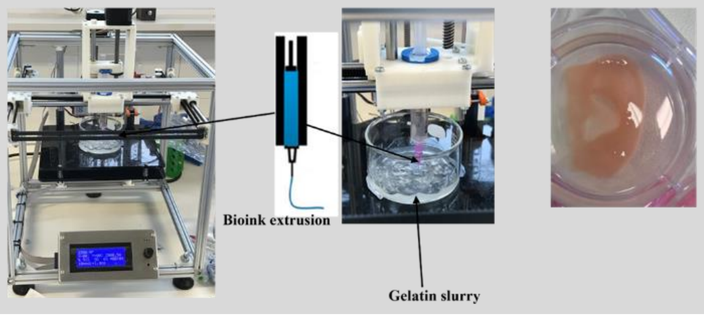
Mechanical properties were also enhanced in composite inks on examining compressive moduli compared to GelMA or AlgMA alone.



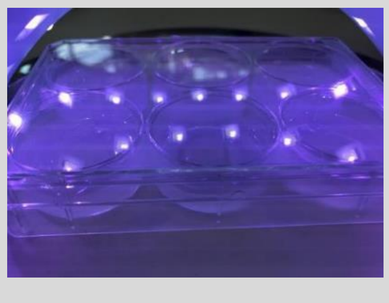


Following bioprinting, constructs underwent dual ionic and UV crosslinking to increase scaffold stability in culture.

$CaCl_2$ and $BaCl_2$ crosslinking in gelatin support bath (modified FRESH method)

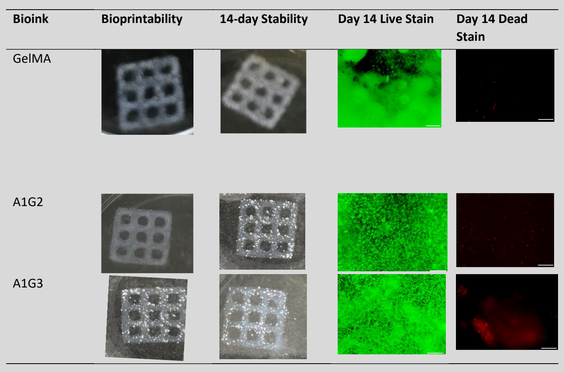


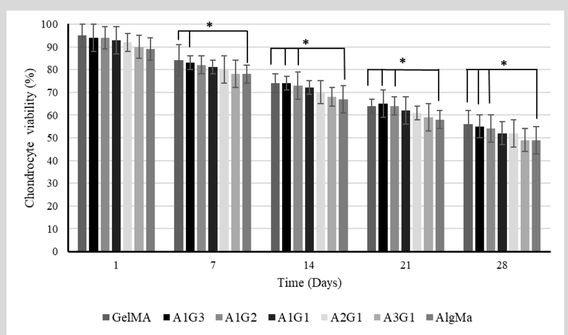
UV crosslinking of scaffolds



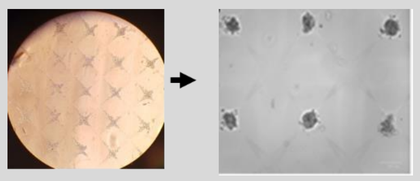
Post crosslinking: high cell viability & robust structure

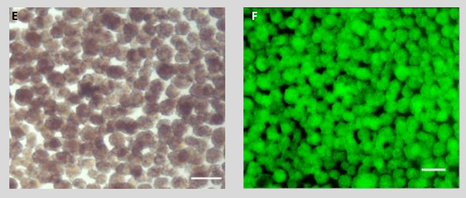
Scaffolds had maintained 3D structure within culture conditions following triple crosslinking. Excellent viability of chondrocytes and MSCs was also seen over 28 days in culture.



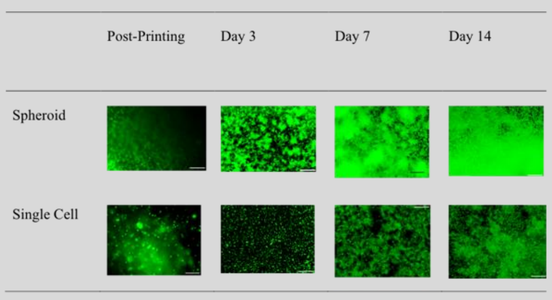


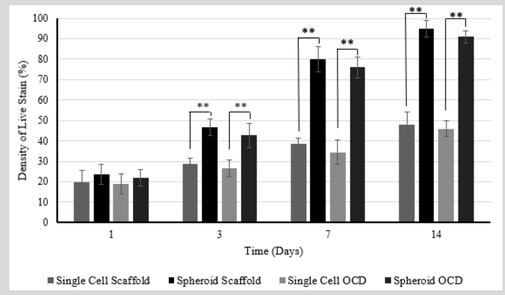
Using cell spheroids within bioinks





Cell spheroids have superior intercellular communication when compared to cells grown in 2D culture. MSC and chondrocyte spheroids were therefore produced via 3D culture added to AlgMa/GelMA bioink in high density (above).



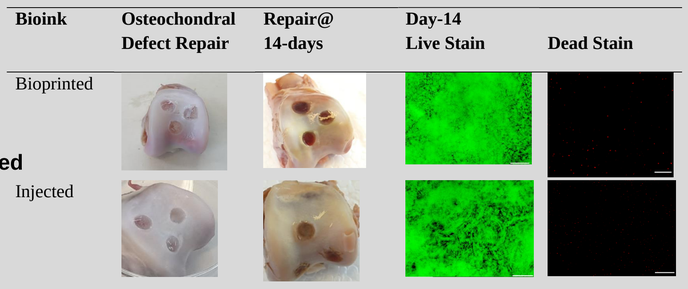


At 3 days onwards of culture, significantly (** $p<0.001$) greater density of cell growth was detected within spheroid containing scaffolds compared to those prepared using single-cell suspension bioinks.

Repairing *in vitro* OCDs with bioink loaded with cells

An *in vitro* OCD model was created and OCDs repaired by injecting or press fitting 3D printed bioink into OCDs. Bioink was ionically and UV crosslinked in situ. After 14 days culture, OCDs remained repaired by the crosslinked bioink, with very high viability and density of growth of chondrocytes and MSCs seen.

OCDs repaired with bioink and then crosslinked



Conclusions

In summary, we have demonstrated:

- A novel bioink (AlgMA/GelMA) that can be triple-crosslinked, facilitating successful chondrocyte and MSC growth following 3D bioprinting.
- The bioinks can be injected or 3D bioprinted to successfully patch up in vitro OCDs.
- Clinically this offers flexibility in being able to tailor repairs to defects in real time with or without use of bioprinting, hopefully showing potential for a new approach to treating AC defects.