A novel method for generating 3D constructs with branched vascular networks using multi-materials bioprinting and direct surgical anastomosis

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Manuscript Authors: Xin Liu, Xinhuan Wang, Liming Zhang, Lulu Sun, Heran Wang, Hao Zhao,

Zhengtao Zhang, Yiming Huang, Jingjinqiu Zhang, Biaobiao Song, Chun Li,

Hui Zhang, Song Li, Shu Wang, Xiongfei Zheng & Qi Gu

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Section No.	Headings	Sentences
Section: 1	Abstract	8
Section: 2	1. Introduction	19
N/A		0

A novel method for generating 3D constructs with branched vascular networks using multi-materials bioprinting and direct surgical anastomosis

S1 [001] Abstract

S1 [002] Vessels pervade almost all body tissues, and significantly influence the pathophysiology of human body.

Vessels pervade almost all body tissues, ...

- ... and significantly influence the pathophysiology ...
- ... of human body.
- **S1 [003]** Previous attempts to establish multi-scale vascular connection and function in 3D model tissues using bioprinting have had limited success due to the incoordination between cell-laden materials and stability of the perfusion channel.

Previous attempts ...

- ... to establish multi-scale vascular connection ...
- ... and function ...
- ... in 3D model tissues ...
- ... using bioprinting have had limited success ...
- ... due to the incoordination ...
- ... between cell-laden materials ...
- ... and stability ...
- ... of the perfusion channel.
- **S1 [004]** Here, we report a methodology to fabricate centimetre-scale vascularized soft tissue with high viability and accuracy using multi-materials bioprinting involving inks with low viscosity and a customized multistage-temperature-control printer.

Here, ...

- \dots we report a methodology \dots
- ... to fabricate centimetre-scale vascularized soft tissue ...
- ... with high viability ...
- ... and accuracy ...
- \dots using multi-materials bioprinting \dots
- ... involving inks ...
- ... with low viscosity ...
- ... and a customized multistage-temperature-control printer.
- **S1 [005]** The tissue formed was perfused with branched vasculature with well-formed 3D capillary network and lumen, which would potentially supply the cellular components with sufficient nutrients in the matrix.

The tissue formed was perfused ...

- ... with branched vasculature ...
- ... with well-formed 3D capillary network ...
- ... and lumen, ...

```
... which would potentially supply the cellular components ...
... with sufficient nutrients ...
... in the matrix.
```

S1 [006] Furthermore, the same methodology was applied for generating liver-like tissue with the objective to fabricate and mimic a mature and functional liver tissue, with increased functionality in terms of synthesis of liver specific proteins after in vitro perfusion and in vivo subperitoneal transplantation in mice.

```
Furthermore, ...
... the same methodology was applied ...
... for generating liver-like tissue ...
... with the objective ...
... to fabricate ...
... and mimic a mature ...
... and functional liver tissue, ...
... with increased functionality ...
... in terms ...
... of synthesis ...
... of liver specific proteins ...
... after in vitro perfusion ...
... and in vivo subperitoneal transplantation ...
... in mice.
```

S1 [007] Moreover, to establish immediate blood perfusion, an elastic layer was printed wrapping sacrificial ink to support the direct surgical anastomosis of the carotid artery to the jugular vein.

```
Moreover, ...
... to establish immediate blood perfusion, ...
... an elastic layer was printed wrapping sacrificial ink ...
... to support the direct surgical anastomosis ...
... of the carotid artery ...
... to the jugular vein.
```

S1 [008] Our findings highlight the support extended by vasculature network in soft hydrogels which helps to sustain the thick and dense cellularization in engineered tissues.

```
Our findings highlight the support extended ...
... by vasculature network ...
... in soft hydrogels ...
... which helps ...
... to sustain the thick ...
... and dense cellularization ...
... in engineered tissues.
```

S2 [010] Three-dimensional (3D) bioprinting techniques have significantly facilitated the process of fabrication of complex, heterocellular soft artificial tissues in vitro, which combine polymeric biomaterials and cells.

```
Three-dimensional ...
... (3D) ...
... bioprinting techniques have significantly facilitated the process ...
... of fabrication ...
... of complex, ...
... heterocellular soft artificial tissues in vitro, ...
... which combine polymeric biomaterials ...
... and cells.
```

S2 [011] [1–3] During the process of bioprinting, the bioinks provide protection to the cellular component, ensuring high cell viability, while also mimicking the extracellular matrix to promote bioactivity.

```
[1–3] ...
... During the process ...
... of bioprinting, ...
... the bioinks provide protection ...
... to the cellular component, ...
... ensuring high cell viability, ...
... while also mimicking the extracellular matrix ...
... to promote bioactivity.
```

S2 [012] [4–6] Although bioprinting technology has shown great potential in tissue engineering, the thickness of constructed tissues was limited to several hundred micrometers due to restricted oxygen and nutrient diffusion, which is integral in maintaining cell viability and proliferation.

```
[4–6] ...
... Although bioprinting technology has shown great potential ...
... in tissue engineering, ...
... the thickness ...
... of constructed tissues was limited ...
... to several hundred micrometers ...
... due to restricted oxygen ...
... and nutrient diffusion, ...
... which is integral ...
... in maintaining cell viability ...
... and proliferation.
```

S2 [013] [7–8] In highly vascularized tissues, such as liver and kidney, the formation of new blood vessels is essential for growth beyond the diffusion limit.

```
[7–8] ...
... In highly vascularized tissues, ...
... such as liver ...
... and kidney, ...
... the formation ...
... of new blood vessels is essential ...
... for growth ...
... beyond the diffusion limit.
```

S2 [014] [9–10] Therefore, building multi-branched perfusable vascular networks is critical to the fabrication of thick tissue constructs.

```
[9–10] ...
... Therefore, ...
... building multi-branched perfusable vascular networks is critical ...
... to the fabrication ...
... of thick tissue constructs.
```

S2 [015] Recent advances in 3D tissue fabrication have led to efficient bioprinting of blood vessels.

```
Recent advances ...
... in 3D tissue fabrication have led ...
... to efficient bioprinting ...
... of blood vessels.
```

S2 [016] [11–12] The strategies followed in these studies can be classified into two main groups: (i) scaffold-based approach, and (ii) scaffold-free bioprinting of vascular constructs.

```
[11–12] ...
... The strategies followed ...
... in these studies can be classified ...
... into two main groups: ...
... (i) ...
... scaffold-based approach, ...
... and ...
... (ii) ...
... scaffold-free bioprinting ...
... of vascular constructs.
```

S2 [017] [13] The first approach can be divided into three major bioprinting modalities which include extrusion-based bioprinting, droplet-based bioprinting, and laser-based bioprinting.

```
[13] ...
... The first approach can be divided ...
... into three major bioprinting modalities ...
... which include extrusion-based bioprinting, ...
... droplet-based bioprinting, ...
... and laser-based bioprinting.
```

S2 [018] [14–15] Extrusion-based bioprinting enables fabrication of macro-vascular constructs (in the order of magnitude of a few centimeters), which allows printing with fugitive inks with subsequent remove for achieving a distinct vascular pattern.

```
... Extrusion-based bioprinting enables fabrication ...
... of macro-vascular constructs ...
... (in the order ...
... of magnitude ...
... of a few centimeters), ...
... which allows printing ...
... with fugitive inks ...
... with subsequent remove ...
```

End of Sample Audit

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