3D printed Radiopaque Bioresorbable Citrate-based Cardiovascular Scaffolds

Northwestern
CENTER FOR ADVANCED REGENERATIVE ENGINEERING

Shivakalyani Adepu[1,2], Cheng Sun[2], Guillermo A. Ameer[1,2]
[1]Department of Biomedical Engineering, Northwestern University, Evanston, IL
[2]Center for Advanced Regenerative Engineering (CARE), Northwestern University, Evanston, IL
shivakalyani.adepu@northwestern.edu

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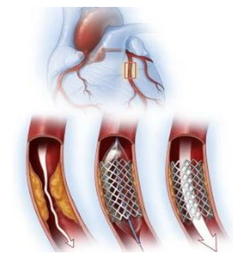
Background



Cardiovascular diseases (CVDs) are a leading cause of death worldwide, with atherosclerosis causing arterial narrowing or blockage due to plaque buildup. Angioplasty restores blood flow using a balloon catheter, with or without stent placement. However, permanent metallic stents can lead to chronic inflammation, late stent thrombosis, and impaired vessel remodeling, motivating the development of biocompatible polymeric bioresorbable stents.

Figure 1. An occluded vessel treated with Angioplasty[1]

Hypothesis

Polymeric stents suffer from poor radiopacity and often require thick struts that increase inflammation and arterial injury. TIBA-functionalized citrate-based mPDC enables intrinsically radiopaque bioresorbable vascular scaffolds (BVS), while µCLIP stereolithography produces thin struts (~80–100 µm) with desirable mechanics and added antioxidant benefit.

Methodology

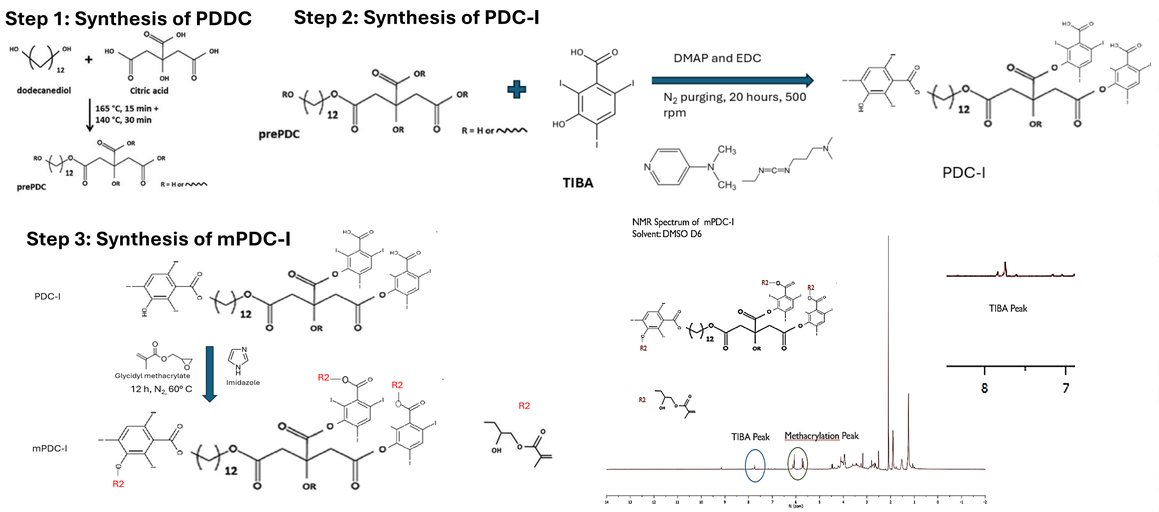


Fig.1 Reaction schematics of functionalization of citrate polymer with TIBA and characterization by NMR

Synthesis of radiopaque citrate polymer

The synthesis procedures of mPDC-I and mTIBA BVS can be divided into 4 steps:

1) Synthesis and purification of PDDC pre-polymer by polycondensation
2) Synthesis and purification of PDC-I by EDC and DMAP mediated esterification
3) Methacrylaton of PDC-I
4) Synthesis of mTIBA by methacrylating TIBA

The reaction schematics is depicted in Figure 1 along with the NMR spectra.

Fabrication of the BVS

Preparation of ink using photo initiators (EDAB and Irgacure)

3D printing by µCLIP stereolithography: UV light induced free radical polymerization of mPDC-I and mTIBA (Figure 2)

Results

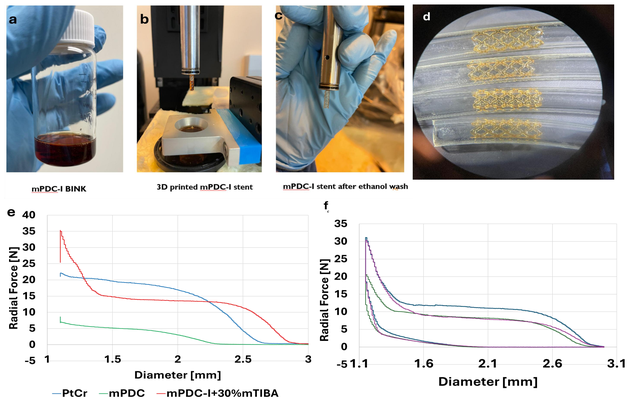


Fig 2. (a) mPDC-I ink, (b-c) 3D printed mPDC-I stent exiting the resin bath (d) mPDC-I 30% mTIBA stents deployed in an artificial blood vessel (e) Crimping tests show that PtCr metal stent and mPDC-I 30% mTIBA stents sustain radial forces of 15N and 13 N without failure up to 1.1mm diameter reduction, while mPDC achieve a 8N radial force and maintain integrity when crimped to a 1.1 mm diameter.(f) Cyclic crimping and expansion

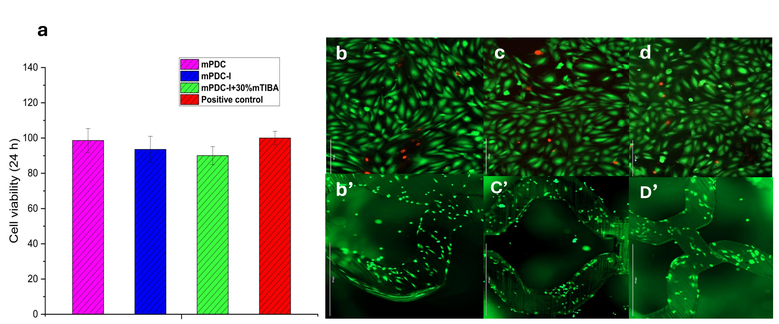


Fig 3. *In vitro* responses of Human umbilical vein endothelial cells (HUVECs) when seeded on to the stents are studied by MTT and live dead assay;
(a) MTT assay shows high cell viability for both mPDC and mPDC-I+30% mTIBA extracts, comparable to the control medium. (b-d) Live/dead assay of HUVECs seeded on mPDC (b&b'), mPDC-I (c&c'), mPDC-I+30% mTIBA (d&d') BVSs confirms good cell adhesion and morphology. (n=3)

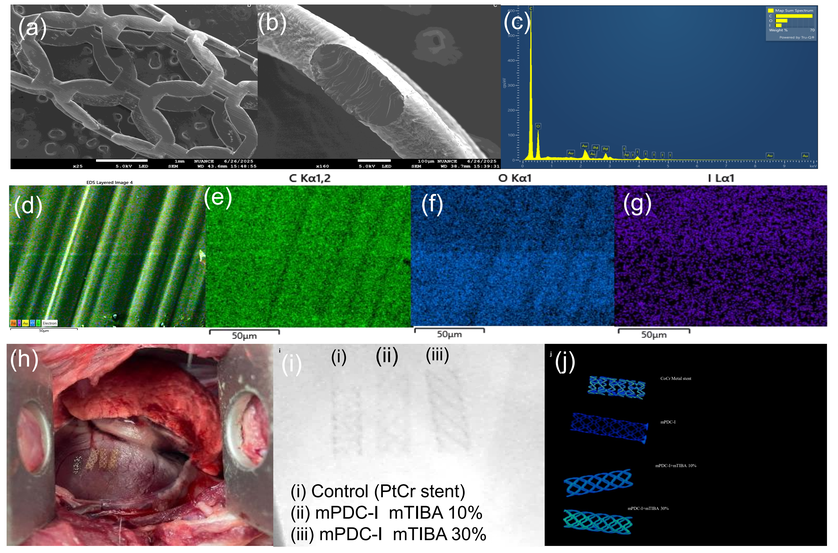


Fig 4: (a-b) SEM images of 3D-printed low-profile (90 µm) mPDC-I+30% mTIBA stents (b) Cross-sectional view and (c-g) EDS compositional analysis validates the presence of iodine within the BVS. (i) EDS spectrum verifies 15% iodine loading by weight. (h) Inserting BVS in a euthanized pig heart and (i) the resulting fluoroscopy imaging further demonstrates its X-ray visibility for in vivo deployments. (j) Micro-CT imaging of mPDC-I+30% mTIBA stents in chicken thigh muscle in comparison with the control CoCr metallic stent.

Conclusions

- The mPDC was successfully functionalized with TIBA by ester linkage and confirmed by NMR and FTIR
- In SEM-EDS analysis, presence of ~10 wt% elemental iodine positively correlates covalent attachment of TIBA
- The mPDC-I stents displayed a greater radial force of ~13N comparable to the metal stent (~15N)
- mPDC-I, mPDC-I+10 and 30% mTIBA BVSs were visualized in both microCT and Fluoroscopy when placed in euthanized pig heart comparable to the metallic stent
- The developed BVSs were found to be biocompatible as demonstrated in the MTT Cytotoxicity Assay with a 90-95 % cell viability
- **Future Work:** *In vivo* evaluation of mPDC-30% INPs stents in porcine model for 28 and 90 days

Acknowledgements

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References

[1] Malloy, T. *Mayo Clinic study looks at changes in patient characteristics, outcomes for coronary revascularization*.
[2] Ding, Y.; Fu, R.; Collins, C. P.; Yoda, S.; Sun, C.; Ameer, G. 3D-Printed Radiopaque Bioresorbable Stents to Improve Device Visualization (Adv. Healthcare Mater. 23/2022). *Advanced Healthcare Materials* **2022**, *11* (23), 2270138.