Vasculitis and Aneurysms

2000 people in the UK are diagnosed with vasculitis every year.[1]

3.2% of the global population are affected by unruptured aneurysms.[2]

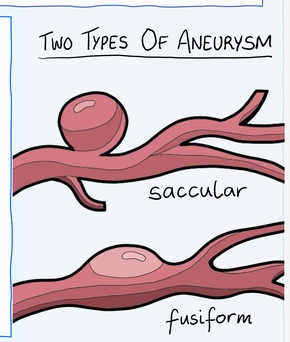
Vasculitis - a group of rare conditions that damage blood vessels by causing inflammation or swelling.

Aneurysm - an abnormal bulge or ballooning in the wall of a blood vessel.[4]

Aneurysms when left untreated may rupture, with major consequences that can be lethal. Several solutions exist, but each come with significant downsides like long recovery durations and lack of effectiveness.

An aneurysm is dangerous as the risk of it rupturing or bursting at any time can cause life-threatening internal bleeding. 50% of cerebral (brain) aneurysms[5] prove fatal as stated by the Brain Aneurysm Foundation.[5]

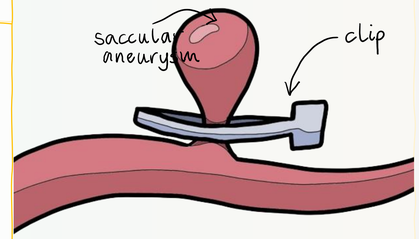
Vasculitis can lead to the development of aneurysms. Conversely, the weakening and damage to blood vessel walls caused by an aneurysm can also trigger an inflammatory response, resulting in vasculitis. Both have the potential to block off consistent supply to vital organs, resulting in serious consequences.



Existing Solutions

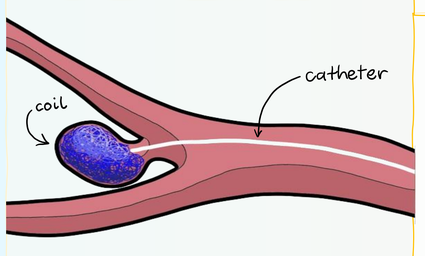
Surgical Clipping

A neurosurgeon (for a cerebral aneurysm) would open the skull and find the affected artery – a metal clip is then installed which prevents blood flow into the aneurysm. However, there is a long recovery duration for aneurysms ranging from 4 to 6 weeks.[6]



Endovascular Coiling

This procedure is less invasive where a flexible wire is fed into the aneurysm using a catheter. The wire coils up inside the aneurysm and seals it up from the artery. However, it isn't as effective as surgical clipping in preventing another aneurysm from potentially occurring.7



These solutions are used when the aneurysm does not need to be removed. However, in instances where the aneurysm must be removed due to the danger of a rupture, this can often change the shape of the vasal wall and can alter the optimal blood pressure in that region due to more/less cross-sectional area compared to the force of the blood flow.

Graft & Grow

ABOUT US:
Noah: Data Research and Citations
Rayyan: Website Creator and Study Designer
Xander: Product Engineer and CAD Renders
Krish: Editor, Surgical Research and Review
Samay: Poster Design, Illustrations and Concept

All illustrations are created by our team.
We are Year 10 biology and engineering enthusiasts from Merchant Taylors' School, Northwood

Scan to visit our website for renders and bibliography!

How It Works

Based on our research we decided to design a 3D printed graft which could fit within a vasal wall between the muscle and the endothelium. This would be applicable to both arteries and veins. Our graft will be used to replace removed aneurysms which have deformed the vasal wall from its original shape and will be manufactured flexibly to ensure that there are no blockages during vasodilation and vasoconstriction.

Our Design and Scientific Research

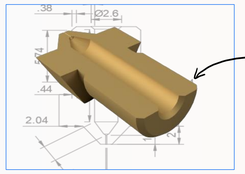
3D Printing and Material Science

3D printing uses a heated nozzle to melt and extrude thermoplastic filament, depositing it in thin layers on a build plate to create complex shapes and geometries. PLA (polylactic acid) is an eco-friendly material made from the polymerisation process of lactic acid, a natural byproduct of our bodies from anaerobic respiration. FDM 3D printing is extremely cost efficient with small parts, such as our graft, each costing less than £0.50. The CT scans are priced at around £450 for private healthcare, however, for the NHS, this procedure would be free.

Graft Placement and Decomposition

The grafts will replace the inflamed blood vasal wall and the body's natural enzymes (produced in the lysosomes of cells) will eventually break the polylactic acid-based grafts into lactic acid, which is either oxidised into carbon dioxide and water, or converted and stored as glycogen in the liver. A newly grown tissue integrates into the adjacent blood vessels via the channels which provide conditions for new tissue to develop. The slow release of lactic acid due to the decomposition of the PLA from our graft would allow for its easy removal from the bloodstream.

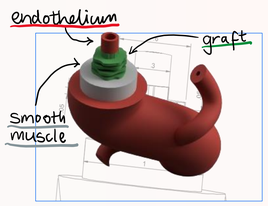
OUR MODEL OF A 3D PRINTER NOZZLE

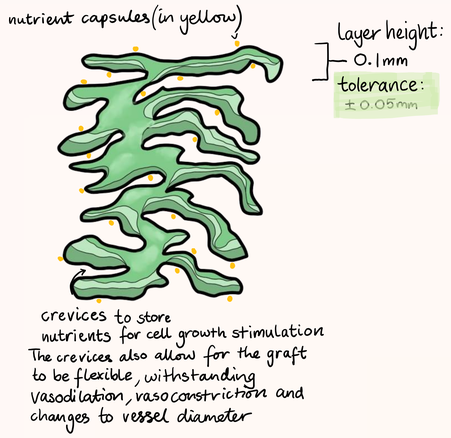


This nozzle is specifically designed to extrude PLA as thin as 0.05mm in diameter

OUR GRAFT IN A BLOOD VESSEL

This is a cross-section diagram of the graft installed in a fusiform aneurysm





These grafts will be loaded with proteins such as growth factor FGF and enzymes to encourage growth of new cells and repair of damaged cells. Vitamin C will be present for collagen synthesis and vitamin B for cell metabolism. These nutrients will be present within the crevices of the graft – which provide an additional benefit of increasing the surface area to attach these nutrients onto.

Hydrogels and Anti-Inflammatory Agents

The grafts will be coated in an amorphous hydrogel which will act as a barrier to prevent small fragments from breaking off during biodegradation, thereby blocking the blood vessels and causing further complications. The hydrogel will provide the grafts with a smooth surface finish which replicates the nature of the endothelium, serving very similarly to human blood vessels. We have selected biocompatible materials, a precautionary step against the patient's body rejecting the graft. However, it is still important to address the risk of unwanted inflammation. We would include the chemical dexamethasone[8], which would temporarily reduce the activity of the white-blood cells surrounding the affected area. There is little chance of contamination as the area and surgery is already fully sterile. The chances of this side-effect would be reduced through this addition.All

Limitations

FDM 3D printing is powerful and flexible but has major limitations. We are using a custom nozzle to have access to 0.1mm nozzle diameter, which is not a standard size for 3D printers. This will allow us to print very small parts, however this means that there is a minimum size for the grafts.

The limitations of 3D printing also limit us to 0.5mm layer heights. Another limitation is that our solution is contraindicated in liver disease as the liver will not be able to transfer and store the lactic acid from the graft.

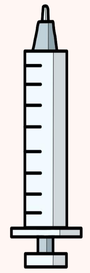
Ethics and Safety

The surgery would be invasive, however to ensure safety there would be monitored sterilisation procedures in place for all equipment used. Ultrasonic cleaners will be used first, then either autoclaving or hydrogen-peroxide plasma sterilisation will be used during this process. These tools will be packaged according to medical standards until use. The mice will be ethically sourced and we will have informed consent based on the effects on the mice before even shifting to human testing. All procedures carried out will comply to the Animals Scientific Procedures Act 1986.

Implementation

Preparation

It will be ensured that the anatomical data of the graft is compatible with the patient; therefore, a CT scan will be performed before converting the imaging data into a 3D scan. CAD software will be used to construct the graft, facilitating the specific details required by each patient using a custom approach. To prepare for the surgery, appropriate anaesthesia will be induced.



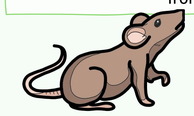
Using Vascular Bypass Surgery

The surgeon will be given the role of determining whether local or general anaesthesia is appropriate based on the scale of the incision. After the incision has been performed to provide access to the affected blood vessel, the vasal walls of the blood vessel will be cut so that the graft can be placed in between the smooth muscle and endothelium. To ensure careful positioning of the graft and reduce patient risk, imaging guiding will be used for precise placement. The patient will be made to stay in hospital for seven days to recover, before being regularly tested monthly for any complications with the integration or decomposition of the graft.

Cohort Study

We are using mice for our cohort study as they are 95% genetically similar to humans and are easy to source. The same species will be used and their environmental conditions from birth will be the same for all mice.

We will use an initial cohort of 30 deceased mice (maximum 24 hours after death to ensure tissue integrity). We will divide the group into two (15 in each): a test arm and a control arm. The mice will have a section of their endothelium and muscle removed from an artery in the same location. The graft will be inserted in the test group whereas the control group will have no graft inserted. A synthetic perfusion system will be used to demonstrate blood circulation through the mice – this will mimic physiological conditions. A micro-CT scan will confirm the placement of the graft and ensure there are no potential leaks from the surgery.



We will be measuring the breakdown product(s) (lactic acid) from the PLA after a period of 4 months, with regular micro-CT scanning in place weekly to monitor the growth of the cells around the graft. The period of degradation of the graft will be measured as the blood-like solution is pumped through at a steady rate. The structure of the grafts will be closely monitored to see if they provide any additional risk to the artery.

To expand the study, we would increase the cohort size to 100 for a more reliable study. We would also use industry standard data management systems to handle large datasets such as REDcap to store and analyse data from large trials, especially if we move from mice to human clients based on the safety and effectiveness of the previous cohort study(ies).