**What is the clinical problem?**

- Intervertebral disc (IVD) degeneration is a leading cause of back pain worldwide.
- Back pain costs the UK economy £12bn annually.
- Existing treatments have poor clinical outcomes.
- Disease models and regenerative therapies are essential, however, IVDs are difficult to replicate using traditional tissue engineering techniques.

**Bioprinting: a novel tissue engineered solution**

- 3D Bioprinters can create multi-material structures using bioinks made from living cells and natural or synthetic biomaterials.
- This project bioprinted IVDs from alginate, collagen, and laminin to mimic the stiffness, biochemical composition, and growth conditions of IVDs at different stages of development, health, and disease.
- More than 120 functional IVDs were created in 2022.

**Key Findings: Bioprinted IVDs show healthy and degenerated tissue formation in different conditions**

**Figure 1:** Healthy and degenerate conditions within the nucleus pulposus (NP) and annulus fibrosus (AF) regions of the IVD.

**Figure 2:** Why use alginate, collagen, and laminin bioinks?

- Alginate is a cell-friendly natural biomaterial that allows regional control over bioprinted IVD stiffness.
- NP and AF cells prefer a collagen-rich environment.
- Healthy IVDs are laminin-rich. Removing it mimics disease.

**Figure 3:**

A) Native IVD with collagen fibres stained red. B) Bioprinted IVD after 35 days in culture. C) The cells produced hyaluronic acid (HA), shown using immunofluorescence staining (IF). Magnified image highlights regional HA production. Computational analysis of IF images (n > 1500) revealed D) stiff, laminin-poor, oxygen-rich (degenerate) conditions reduced HA production, whilst E) healthier conditions lead to greater amounts; findings were verified using F) aggregan, G) collagen, and other IVD proteins.

**Impact: World-first demonstration of a bioprinted whole organ IVD model**

- Bioprinted IVDs accurately mimicked the structure of real (native) IVDs.
- Tissue stiffening generally reduced protein production in healthy NP & AF cells.
- Laminin caused NP cell clustering, commonly seen in young NP cells.
- Healthy, low-oxygen growth conditions resulted in rapid IVD tissue formation.

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