From Keyboard to Clinic: Computational Trials of Regenerative Therapy Safety in the Human Heart

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WHY we are interested

One UK heart attack **hospital admission every 5 minutes**[1]

Heart attacks cause **irreparable scarring** of the affected tissue

Coronary heart disease costs the NHS **£1,500,000,000 per year**[2]

Computational trials are a fast and precise tool to ethically investigate new treatments

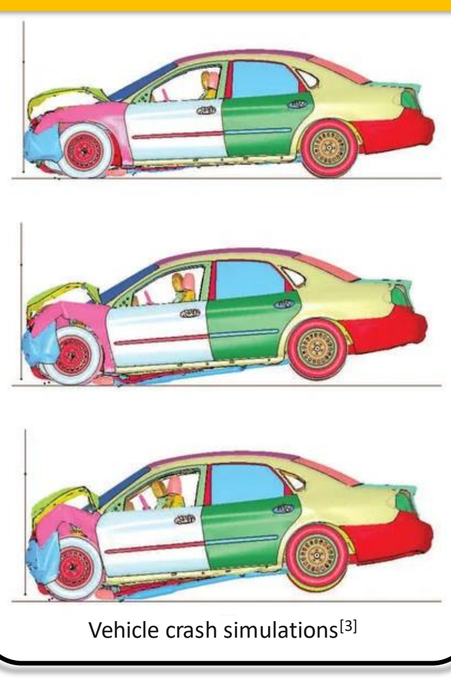
Stem cell injection may renew the damaged heart

Stem cell injection can improve cardiac function, however, the stem cells are immature and **might disturb the heart's rhythm: is it safe?**

HOW we do it

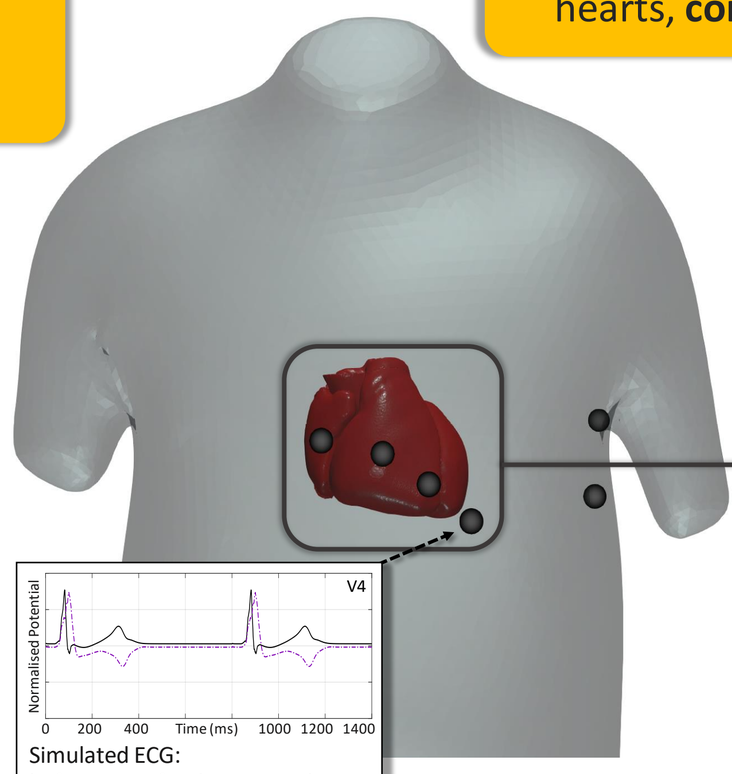
Simulation: Body → Organ → Cell

Computer simulations are routinely used to **test new inventions and their safety** across many sectors

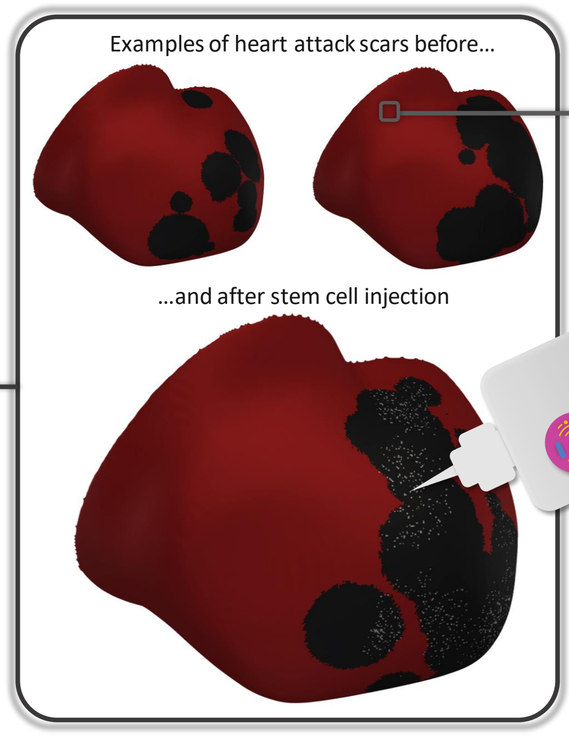


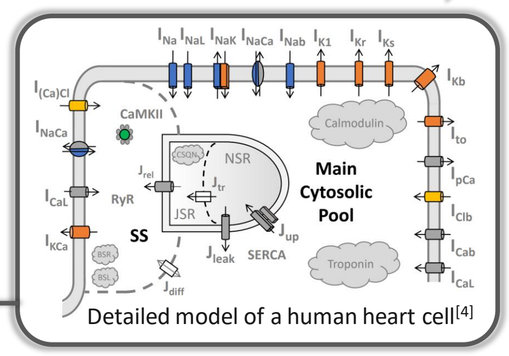
Vehicle crash simulations[3]

Cardiac digital twins are virtual copies of human hearts, **constructed from real patient data**



Simulated ECG:
before — after heart attack - -

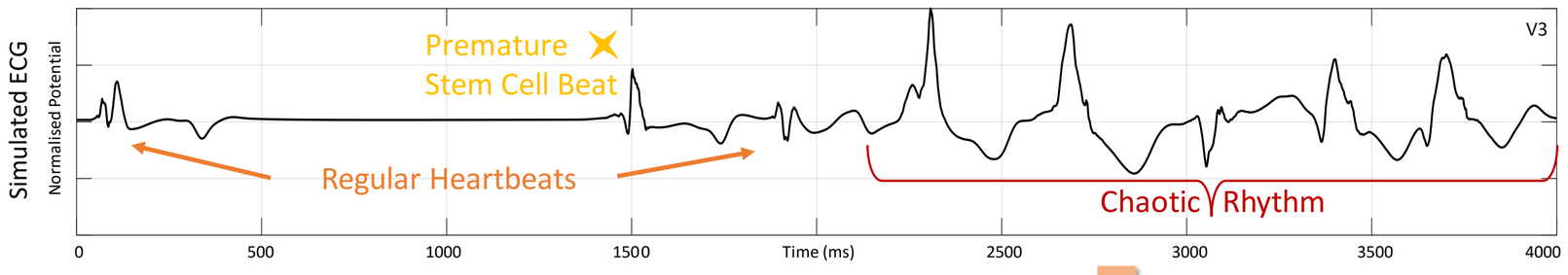




Detailed model of a human heart cell[4]

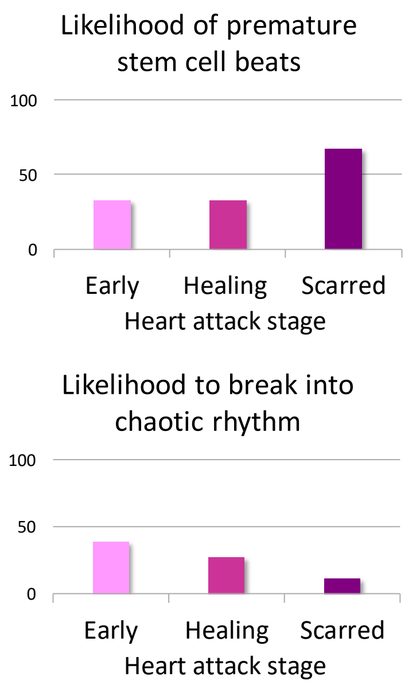
We **simulate stem cell injection** in the scarred human heart to **investigate potential side effects**

WHAT we found

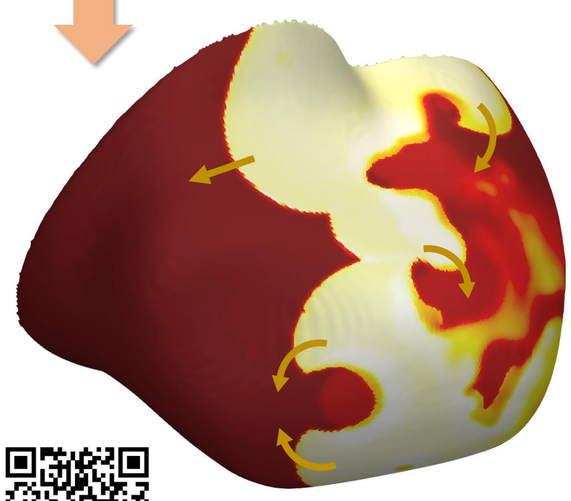


To **guide clinical delivery**, our **mechanistic investigations** showed:

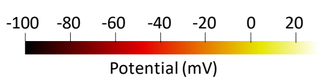
1) **Healed heart attack scars** promote stem cells to produce **extra beats**
2) **Early after a heart attack** following break out into **chaotic rhythm** is favoured



Mechanistic investigation of chaotic activity



Video of chaotic episode



IMPACT

+ Efficient and safe exploration of optimal delivery strategies, such as injection location and cell dose
+ Large-scale investigations of safety in individual patients and different disease characteristics
+ Systematic drug discovery and design to improve therapy safety whilst maintaining efficacy

Our **modelling and simulation framework** can be used **for safety and efficacy evaluations** to advance therapy development, delivery **and mitigation of safety concerns**

References

[1] BHF Factsheet 2024, https://www.bhf.org.uk/-/media/files/for-professionals/research/heart-statistics/bhf-cvd-statistics-uk-factsheet.pdf

[2] Heart and Circulatory Disease Statistics 2021 – Chapter 4, Table 4.9, https://www.bhf.org.uk/what-we-do/our-research/heart-statistics/heart-statistics-publications/cardiovascular-disease-statistics-2021

[3] Munyazikwiye et al., *Designs* (2018), https://doi.org/10.3390/designs2040043

[4] Tomek et al., *eLife* (2019), https://doi.org/10.7554/eLife.48890

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