10 Epilogue: Where Can Extreme Tissue Engineering Go Next?

10.1 So where *can* extreme tissue engineering go next? 247

Half of my students advised me, 'Under no circumstances do a crystal-ball-gazing, what-the-future-holds section!' Tradition has it that when this comes from wrinkly established scientists, it is at best embarrassing and at worst off-putting.

This has merit. There is clearly a tendency on one hand to predict wildly optimistic or over-ambitious progressions for your view and ideas (after all, you will be retired before anyone proves you wrong!). But on the other hand, crusty guys who are joined at the hip to the core concepts *can* actually have a privileged view of the log-jams and off-track opportunities before they become obvious.

I decided to take-the-advice-but-not (a Manchurian compromise). Here is the section on 'futures' – but notice how short it is. This is because this particular question needs little analysis to find its answer.

10.1 So where *can* extreme tissue engineering go next?

The simple, first-level answer is 'Nowhere – it will end'. Nothing in science stays *extreme* for very long. The 'extreme' part implies that it is at the frontier – rough, partly understood, partly surprising, presently untamed. This is good for science and bad for technology and translation, whether industrial or clinical. From history, we know that either such areas are tamed and become useful, or they remain ambiguous, with limited capacity to translate to our target aspirations. Ambiguity, surprise and randomness are the stuff of sports and the arts. Olympic tissue engineering is not going to happen soon, although tissue engineering in the Olympics is coming and may already be with us.

No, extreme tissue engineering (ETE) is a useful concept now but, by its very nature, it will need to be reassessed in years to come, as it will either have become *not particularly extreme* (i.e. useful and tamed – and so a rubbish title for the 2nd edition), or '*chronically extreme*' (and thus not a useful, translatable scientific field). However, given its present trajectory, I cannot see the latter (becoming not useful) as remotely likely to happen.

Now, we know perfectly well what happens to successful fields in science. They become channelled, socialized and subdivided. So we are likely to see sub-divisions, perhaps into 3D tissue model-, graft- and drug release depot-engineering; cell-rich and matrix-rich tissue engineering; human, veterinary and plant tissue engineering! Given time and enough productive success, some of these sub-divisions will establish their own international societies, journals and perhaps even the odd specialist journalist.

Extreme Tissue Engineering: Concepts and Strategies for Tissue Fabrication, First Edition. Robert A. Brown.

By then, ETE will be gone, because its concepts will have become useful and familiar – so not extreme. At that point, it will be one of you, the readers of *this* extreme, who will be able to tackle the new 'extreme' that you will inevitably find.*

* This is no more than Thomas Kuhn's view of: '*The Structure of Scientific Revolutions*'. Discussed by M.R. Foster (1998) 'Guide to Thomas Kuhn's The *Structure* of Scientific Revolutions' (http://philosphy.wisc.edu/foster/220/kuhn.htm).

To briefly summarize, there may be signs emerging of a strategic track which could take us towards that horizon. This comes from an increasing awareness that we should *actually take control*. That means *making* the 3D tissue structures ourselves, rather than relying ever more on our cells. This is the idea that we should have confidence in the abilities of our tribes, *in collaboration*, to fabricate things directly: ourselves.

However, 'direct fabrication' involves learning:

- how to layer and assemble *native* tissue layers, zones and domains, not as one big, porous lump;
- how to build up structures as a continuum across different scale-hierarchies, not as a series of distinct levels;
- how to analyze and recapitulate our target tissues in terms of their (an)isotropy *in all three planes* rather than the two planes we find in textbook histological slices.

It means discovering:

- how bio-simple we can get away with, rather than how bio-complex we can make things;
- how to support the cells with a tissue-fabric or matrix of an appropriate native protein, so that they *are* tissues from t_{zero}, rather than temporary templates;
- how to make the tissue with its cells *in place* from t_{zero}, rather than toiling with seeding stages;
- and so how to fabricate, *but* only using non-lethal conditions.

In effect, these can be summarized as setting our goals so that **our cells get a job with vacations, rather than a sentence of hard labour**.

These are undeniably high targets, but at least where we fall little short, the tissues that we *can* make will still be impressive. We shall have avoided the trap of aiming low and still missing.

This, then, was the Manchurian compromise, between 'do' and 'don't' offer a glimpse into the future. The prediction of this wrinkly scientist is that *you* or *your colleagues* will define the next stage of extreme tissue engineering, providing that *this* stage stimulates enough of you to dream outside of you speciality.

Hopefully, both groups of my students will be happy with this compromise epilogue.