**Time to retract Lancet paper on tissue engineered trachea transplants**

We call for retraction of the 2008 Lancet article on “clinical transplantation of a tissue-engineered airway” by Macchiarini and colleagues.1 The paper received international media coverage as the “World’s first tissue engineered organ transplant” and on the BBC an author, Professor Martin Birchall, claimed “in 20 years time, virtually any transplant organ could be made in this way”.2 Reality did not match the hype because nearly all subsequent patients who received “tissue engineered airways” died.3 The Lancet was informed in May 2018 that key findings made in the article are false. Despite this, and subsequent demands for retraction of the paper by us and others, the Lancet has refused to do so, without providing any explanation.

The 2008 article reports a human cadaveric trachea was decellularised and colonised with “stem cells” from the recipient. The graft replaced a stenosed left main bronchus. Two sentences summarised the claims: “The graft immediately provided the recipient with a functional airway, improved her quality of life, and had a normal appearance and mechanical properties at 4 months. The patient had no anti-donor antibodies and was not on immunosuppressive drugs.”1

In July 2018, Professor Castells, the newly appointed Medical Director of the Hospital Clinic Barcelona where the operation was performed, wrote to one of us (in response to emails from PM) that in May 2018 he sent an email to inform the Lancet "three weeks after the airway transplantation procedure, it was necessary to stent the transplanted bronchus, due to an homograft collapse".4 Therefore the graft could not have had “a normal appearance and mechanical properties at 4 months.” Castells also informed the Lancet that there were discrepancies in the claims made regarding lung function improvement.

Castells informed us that permission to perform the airway transplantation was granted by the hospital’s ethics committee on 2 April 2008 and by Catalan authorities on 18 April 2008.5 Pieces of the patient’s nasal and bronchial epithelium for so-called stem cell production were received in Bristol University on 1 April 2008, i.e. before ethical approval was granted.5.6 The “tissue-engineering” in Bristol was organised by Professor Martin Birchall, Macchiarini’s co-principal investigator. It happened in a building that was not licenced under the Human Tissue (Quality and Safety for Human Application) Regulations 2007.7

Following our complaints to Parliament’s Science and Technology Committee, its Chair, Norman Lamb MP repeatedly complained to the Lancet’s editor, Dr Richard Horton. On 7 March 2019 Norman Lamb wrote again saying “The Director of the Hospital Clinic in Barcelona wrote to the Lancet in May 2018 to highlight problems with the 2008 paper.…..Your response does not give me confidence that this issue is being handled appropriately, or with sufficient urgency…..The risk to human health of mis-reported patient outcomes surely means that there is a need for the Lancet to be proactive on this issue….. The Lancet has faced criticism in the past about failure to retract unreliable research in a timely manner. Lives are genuinely at risk if inaccurate research is allowed to persist in the published record without at least a ‘statement of concern’ from the publisher.”8

On 14 March 2019, Dr Sabine Kleinert, Senior Executive Editor of the Lancet, wrote to Norman Lamb MP saying “We have asked the UK-based authors of the 2008 paper for a response to the issues raised in the [Newsnight] programme and to Dr Wilmshurst’s concerns. Once we have their responses we will decide what the appropriate next steps are.”9 Despite Freedom of Information requests, we have been unable to locate any copies of subsequent correspondence between the UK authors and The Lancet.

On 4 March 2019, at the invitation of the Lancet editors, the journal published a clinical update letter by Dr Laureano Molins, who treated the patient after Macchiarini left Barcelona.10 The letter says “3 weeks after the transplantation, it was necessary to stent the transplanted bronchus because of a homograft collapse”. It also says subsequently she needed multiple stent placements and eventually had a left pneumonectomy. It fails to report the discrepancy acknowledged by Castells, between the patient’s lung function as per hospital records and the data reported in the 2008 paper.

Journals publish letters of correction from authors when inadvertent errors in publications are discovered. That is not the case here. The letter is not from an author and differences between the claims in the paper and the letter are too great to believe they were the result of error. We believe that the way that the Lancet and the Hospital Clinic Barcelona handled this situation suggests they wished to avoid denouncing the 2008 paper to protect their reputations.

After publication, Macchiarini moved first to the Careggi University Hospital in Florence and, in September 2010, to the Karolinska Institute in Sweden. From 2010 to 2015, Macchiarini was also on the UK Medical Register and he was honorary professor at UCL, to where Birchall had moved.

In 2011, Macchiarini and members of the UCL team switched from cadaveric to plastic tracheal transplants. A 2014 UCL Impact Case Study says this was because decellularising the tracheas risked damaging their underlying structure, “leading to their collapse once they are implanted in the patient”.11

The 2008 paper was foundational in the field, and has lent support to future clinical care and research. However, the collapse of decellularized cadaveric tracheas contributed to the deaths of several patients, including a 19 year old woman who was referred by University College Hospital to Careggi for trachea transplantation with NHS funding, and a 15 year old girl who died 15 days after trachea transplantation at Great Ormond Street Hospital.3 UCL’s website claimed the latter operation was a success.

The Karolinska sacked Macchiarini in 2016. He was found guilty of research misconduct by Sweden’s Central Ethical Review Board, which requested retraction of six papers resulting from Karolinska research. Sweden created a National Board for Assessment of Research Misconduct (NPOF) in the aftermath of the scandal. Macchiarini received a prison sentence from an Italian Court in his absence in 2019.12 The Swedish Public Prosecutor indicted Macchiarini for aggravated assault on patients in 2020, and he is expected to stand trial in 2022.

Since moving to UCL, Birchall has received approximately £10 million of UK and EU funding to continue research into airway transplantation. But despite multiple requests to UCL and Birchall to retract the 2008 paper, neither have done so.

The time has come to retract the paper.

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