Swiss Transplantation Society

Newsletter Summer 2019

Dear STS members and dear Colleagues interested in the world of transplantation. You will find here some highlights of the last STS congress in Thun, and we invite you to participate to the STS congress for next year. Our scientific committee lead by Prof. Hendrik Tevaearai has worked hard to complete once again an interesting programme. The main themes on the conference will be on biological markers in transplantation, xenotransplantation, obesity and transplantation.

On behalf of the STS committee

Prof. Maurice Matter

STS Post graduate course 2019

For the first time the STS Committee decided to organize a postgraduate course the Wednesday before the STS Congress. The course reviewed the following topics: Organisation, patients, law and ethics for Transplantation in Switzerland (F. Immer), Immunology and immunosuppression (J. Villard), Cancer and transplantation: what to screen? (I. Binet), Problems and long-term management in organ transplantation - abdominal organs: kidneys (S. Schaub) and liver & pancreas (A. Andres), - thoracic organs: heart (MJ Wilhelm) and lungs (A. Koutsokera).

The course limited to 20 was attended by 13 participants and well-received. They appreciated the course with an overall speakers'evaluation of 8.6/10 and a general impression of 9.1/10. Among 11 participants who answered the question "would you recommend the meeting to another colleague?" : all said yes.

So this course will be organized the same way in 2020.

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STS awards

We congratulate all those who contributed to the high scientific level of the STS meeting through their work and received the STS 2019 awards:

Clinical awards:

1. First prize (2'500.-): **Dr Xavier Müller**, Zürich. "*Outcomes of DCD liver transplantation using organs treated by hypothermic oxygenated perfusion before implantation*", J Hepatol. 2019;70:50-57

2. Second prize (1'500.-): **Dr Lina Quteineh**, Lausanne. "*Genetic immune and inflammatory markers associated with diabetes in solid organ transplant recipients*", Am J Transplant. 2019;19:238-246

3. Third prize (1'000.-): **Dr Peter Schreiber**, Zürich. "*Metagenomic virome sequencing in living donor-recipient kidney transplant pairs revealed JC Polyomavirus transmission*", Clin Infect Dis. 2018

1.  2.  3. 

Laboratory Research awards:

1. First prize (2'500.-): **Dr Graziano Oldani**, represented here by Prof Toso, Genève. "*Chimeric liver transplantation reveals interspecific graft remodelling*", J Hepatol. 2018;69:1025-1036

2. Second prize (1'500.-): **Dr Daniel Sidler**, Bern. "*The TWEAK/Fn14 pathway is required for calcineurin inhibitor toxicity of the kidneys*", Am J Transplant. 2018 Jul;18(7):1636-1645

3. Third prize (1'000.-): **Dr Maria N. Sanz**, Bern. "*Cardioprotective reperfusion strategies differentially affect mitochondria: Studies in an isolated rat heart model of donation after circulatory death (DCD)",* Am J Transplant. 2019 Feb;19(2):331-344

1.  2.  3. 

Application for the next STS congress is now open. Information is available under https://swisstransplantationsociety.com/award/

Honorary Award and STS excellence award

The 2019 STS honorary member was awarded to **Prof. Alois Gratwohl**, Basel, for his worldwide expertise in stem cells medicine (1). The 2019 STS excellence award was awarded to
Prof. Stefan Schaub, Basel for his outstanding efforts in clinical and basic research in kidney transplantation and immunology (2).

1.  **2.** 

Application and rules for both STS Excellence award (20'000.-) and STS innovation award (10'000.-) are available on our website

https://swisstransplantationsociety.com/sts-excellence-award/

https://swisstransplantationsociety.com/sts-innovation-award/

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Selected summaries from the 2019 STS annual meeting

Organ trafficking: is Switzerland concerned?

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Switzerland already has a solid legal basis against organ trafficking. Up to now no one has been convicted by a Swiss court for organ trafficking. Switzerland participated actively in the elaboration of the Convention of the European Council against organ trafficking and signed it in November 2016[1]. The Convention complements the measures that Switzerland has already put in place at a national level and improves international co-operation.

The implementation of the Convention in Swiss law requires only isolated adjustments to the Transplantation and Human Research Act. In particular, cases of organ trafficking committed abroad by persons who live in Switzerland will also be punishable. It is likely that the Federal Council will submit the dispatch for the approval of the Convention to Parliament in the second half of 2019.

The Organ Trafficking Convention is supplemented by Resolution CM/Res(2013)55 of the Council of Europe[2] which recommends governments to investigate, how many people travel abroad for a transplantation and in which countries these transplantations are carried out. In Switzerland, the first survey took place in 2018. In 2016 and 2017, four people were reported to have travelled abroad for a kidney transplant. The data is part of an international survey by the Council of Europe. The results should be available by the end of this year.

[1] www.bag.admin.ch/organhandelskonvention

[2] www.edqm.eu/sites/default/files/medias/fichiers/resolution_cmres201355_on_establishing_procedures_for_the_collection_and_dissemination_of_data_on_tr.pdf

The Challenge of starting a DCD heart transplant programme

Stephen Large MA MS MRCP FRCS FRCS(CTH) MBA PAE(RCP) on behalf of the New Royal Papworth Hospital DCD heart transplant group

Heart transplantation adds extraordinary value to the recipient by increasing prognosis significantly (8% 2year survival transformed to 85%) and quality of their lives in that 80% of recipients are living independent lives at 5 years after receiving their transplant. However, waiting lists continue to rise and transplantation is increasingly directed towards urgent patients. Overall, rough calculations suggest that there is a 50% chance of being transplanted once on the UK waiting list for a donor heart. During our reflections on this burgeoning gap between demand and supply of donor hearts we noticed that colleagues transplanting abdominal organs were increasingly interested in a new resource. They were interested in donation after withdrawal of futile treatment leading to cardio-respiratory arrest in 2/3rds of patients within 4 hours. These patients undergo a circulatory determined death (DCD) (Maastricht 3). Asking the question "could such donation be of value to those in heart failure" we found 7 interesting points:

A history of cardiac arrest in heart beating, brain dead doors appeared not to affect either short or long-term outcomes after heart transplantation (Ali et al EJCTS 2007)

Hearts could be re-animated in both small and large animal models following modelling for DCD heart donation, albeit within a relatively short time-frame. Our model assumed a normothermic anoxic insult to the heart and relied on pressure-volume measurement of ventricular function showing at least as good an outcome as modelled brain-dead donation.

Modelling in the rat suggested that that window of resuscitation was about 30mins. Our findings followed those of Ganote and colleagues (AmJPath 1975) 45 years ago. Myocyte loss following reperfusion after normothermic ischaemia in the rat heart began after 30mins and was complete by 55mins.

In 2006, we were fortunate to model DCD heart resuscitation of the human heart within a 53year old woman who had suffered a near lethal brain injury as a result of an intra-cranial bleed (Ali JHt&LTx 2009).

We concluded that the DCD heart is primarily ischaemic and restoration of a blood supply resulted within 30mins recovery of cardiac function. There was evidence of good contraction in the DCD resuscitated heart but also loss of structural protein. There was a measured catecholamine storm associated with DCD donation, much larger than that of brain dead donation.

The key challenge was then how to restore a blood supply to the DCD heart (see figure 1 below). Two ways have been described:

Direct procurement and placement on to the blood primed Langandorff rig. This is commercially available as the Organ Care System (Transmedics®) and is termed Direct Procurement (DPP) and restoring a blood supply within the donor by normothermic, regional (in that a blood supply was directed towards the organs of the chest and abdomen only), perfusion or NRP. The latter, although more ethically and manpower demanding had the advantage of restoring a blood supply swiftly, to the organs of interest.

We began our clinical programme in the late hours of 28th February 2015 shortly after 2 developments. Firstly, the definition of DCD death by Academy of the Royal Colleges following wide public consultation (see fig 2) and secondly after Australian colleagues had reported 3 cases of DCD heart transplantation by DPP in late 2014. We have transplanted 65 patients in addition to transporting further, paediatric heart to colleagues in Newcastle-upon-Tyne. The results are at least as good as transplantation from heart beating or DBD heart transplantation and certainly better than accepting death on the waiting list for a suitable heart. In addition, honouring the donors last wish and abolishing ischaemic cholangiopathy that had plagued early DCD liver transplantation.

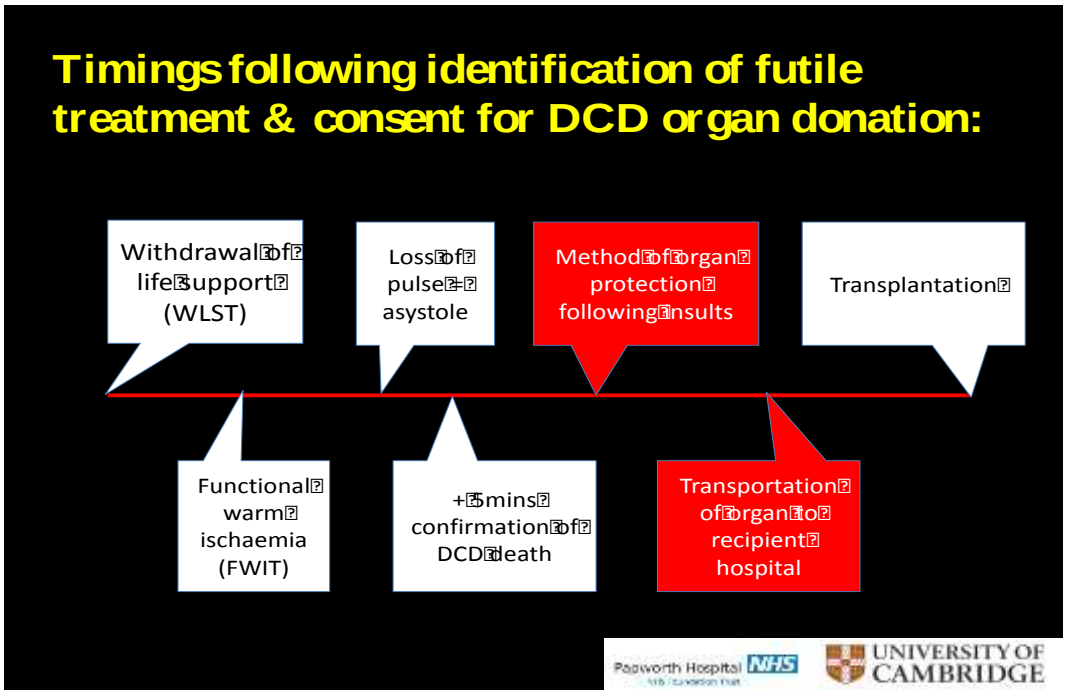

figure 1 showing the sequence of events after withdrawal of futile treatment resulting in ischaemic cardiac arrest and subsequent heart resuscitation

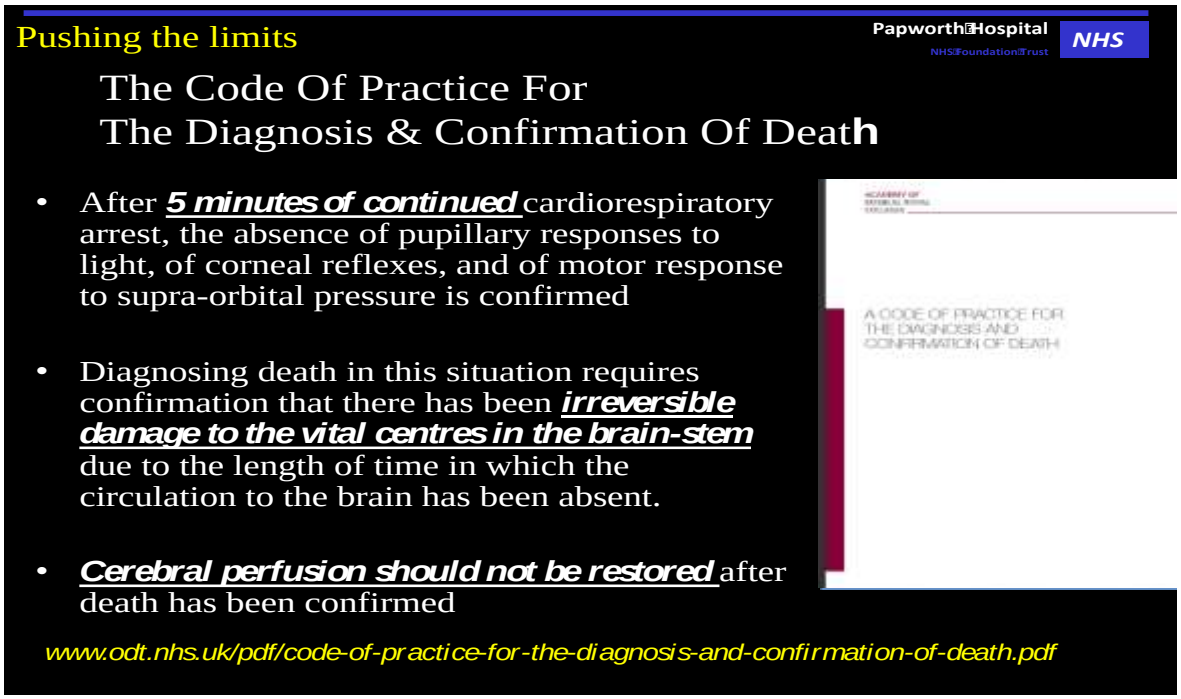

Figure 2 summarises the central conclusions of the Academy of Royal Colleges defining death after treatment withdrawal in futile patients where there is consent for organ donation.

Artificial Intelligence: A New Tool in Transplantation

Dorry Segev, MD PhD
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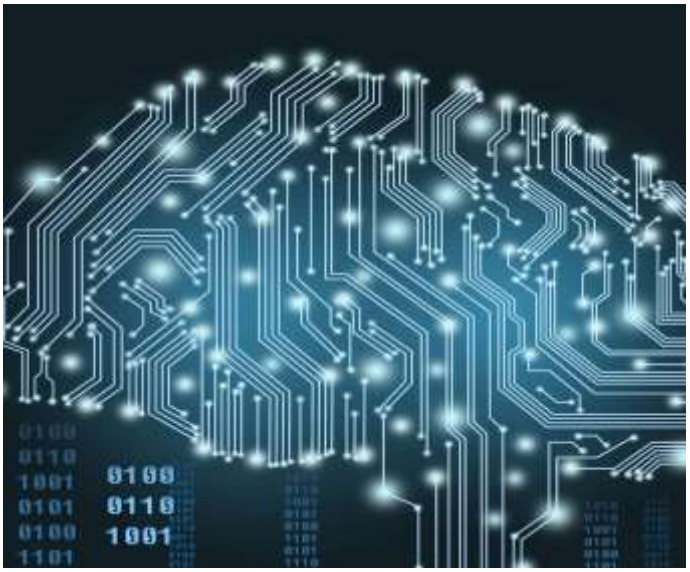

Artificial intelligence (AI) can be defined as the science of getting computers to learn and act like humans do, and improve their learning over time in autonomous fashion, by feeding them data and information in the form of real-world observations. Interestingly, AI is hardly new (the first conference was in 1955), but exponential growth in both healthcare big data availability and computing power has brought about an AI revolution in medicine.

The field of transplantation, with highly organized large-scale registries and linkages to novel data sources such as insurance claims, pharmacy claims, and national death files, has taken advantage of some AI technologies, but we still have opportunities to do more. Classification of techniques such as regression modeling, classification trees, random forests, and neural networks all somehow fall under the umbrella of AI or Machine Learning (ML). All of these techniques are limited by the underlying data, which must be very clearly understood by the investigator to avoid pitfalls such as nonrandom missingness and confounding by indication. That said, the data are inherently automated or mandated, often making them even more reliable than expensive, research-focused primary data collection.

At the Swiss Transplant Society meeting, we discussed some examples of AI/ML in transplantation, many of which are implemented for real-world use at www.transplantmodels.com. We showed how linkage of transplant registry data (the SRTR living kidney donor registry) to national death data and national ESRD data facilitated a data-driven risk prediction framework for living kidney donors (Massie JASN 2017), recently endorsed by KDIGO. We also discussed examples of survival benefit analysis (is your outcome better if you accept the current organ offer or wait on the list for a presumably better one down the road), donor/recipient matching to minimize the harmful effects associated with a suboptimal organ, and Markov decision-process modeling to integrate data from various sources.

As data availability, computing power, and methodologic creativity continue to grow, so will our ability to practice medicine intelligently and empirically.

Editorial commentary

Organ donation : contrary winds in sight ?

John-David Aubert, associate professor
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On a first look, organ donation in Switzerland appears to follow a favourable trend: the total number of donors has increased, mainly due to the development of DCD programs, and with 18.6 donors / million inhabitants is not far from the goal of 20 proposed by the FOPH. For the first time last year the number of patients on the waiting list has slightly decreased for all organs including those waiting for a kidney. On the other hand the popular initiative on the presumed consent for organ donation after death has reached the threshold of 100'000 signatures. This text and/or a softer version elaborated by the federal government will be therefore submitted to vote in the coming years. Finally the creation of the national registry of potential donors by Swisstransplant is a growing success.

However, the Swiss population does not unanimously share the enthusiasm for organ transplantation. For example, the episcopal conference of the swiss bishops, though not opposed to organ donation itself, has publicly taken position against presumed consent. More radical in their views, an association created by health care providers, Aepol (https://www.aepol.net/) is denying the validity of the brain death definition, arguing that death is an evolving process that ends up when every cell of the body is no more viable. By transposing the definition of death from the organ (i.e. the brain) to the cellular level, these activists claim that organ harvesting in either a DBD or a DCD donor is an unethical disturbance of the natural process of dying. This extreme position has recently received indirect scientific support from a much-publicized article in Science where researchers have shown some neuronal activities in pig's brain perfused ex vivo. One could develop the arguments of Aepol even a step further and propose that a body is really dead when not only all the cells but all the genomic DNA is destroyed, as DNA is really the basic brick of Life. This conception would bring back "alive" several Egyptian mummies together with some of our Neanderthal cousins!

As transplant physicians it would be understandable to react emotionally to such statements and to publicly mock their proponents. I do not think this attitude would serve the cause of transplantation. In this debate, our most persuasive advocates are our transplanted patients. By his-her mere physical presence and testimony, an organ recipient may have a much stronger impact on the public than any verbose speech. And in these challenging times our

upmost important task is to ensure that the whole process of organ procurement and allocation is guided by irreproachable clinical procedures in every circumstance.

See you on the next STS annual meeting that will take place again in Thun on January 23rd and 24th 2020 in a partially renewed Congress Hotel Seepark!

https://swisstransplantationsociety.com/meetings/

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