NHS BLOOD AND TRANSPLANT
ORGAN DONATION AND TRANSPLANTATION DIRECTORATE
RESEARCH, INNOVATION AND NOVEL TECHNOLOGIES ADVISORY GROUP MEETING
Wednesday 3 November 2021 from 09:00 – 13:00, via Microsoft Teams

MINUTES

Attendees:

Gavin Pettigrew	GP	Chair, RINTAG
Liz Armstrong	LA	Head of Transplant Development, OTDT
Adam Barley	AB	Specialist Nurse - Organ Donation (Guest)
Marius Berman	MB	Associate National Clinical Lead, Organ Retrieval
Sarah Cross	SC	QUOD National Operational Coordinator
Clare Denison	CD	Head of Integration Programme, OTDT
Aileen Feeney	AFe	RINTAG Lay Member
Andrew Fisher	AFi	NIHR BTRU Representative
John Forsythe	JF	Medical Director, NHSBT
Victoria Gauden	VG	National Quality Manager, NHSBT
Dan Harvey	DH	National Innovation & Research Clinical Lead, OTDT
Joanne Hughes	JH	Specialist Nurse - Organ Donation (Guest)
Emma Lawson	EL	Research & Innovation Manager, NHSBT
Debbie Macklam	DM	Senior Commissioning Manager, NHSBT
Liz Middlehurst	LMi	Head of Operations, Organ Donation
Lorna Marson	LMa	UKODTRN
Lisa Mumford	LMu	Head of OTDT Studies, NHSBT
Ulrike Paulus	UP	Consultant Haematologist, Tissues and Cell Donation and Transplantation
Rutger Ploeg	RP	Director of QUOD
Karen Quinn	KQ	Assistant Director, Service & Commissioning Development, NHSBT
Paul Rooney	PR	Head of Research & Development, Tissue and Eye Services
Maggie Stevens	MS	Specialist Nurse for Research, OTDT
Doug Thorburn	DT	Chair, Liver Advisory Group
Hannah Tolley	HT	Research Project Manager, NHSBT
Steve White	SW	Chair, Pancreas Advisory Group
Steve Bloor (Item 6.1)		
Hazel Lofty (Item 6.1)		
Aaron Ranasinghe (Item 4)		
Rajamiyer Venkateswaren (Item 16)		

Apologies:

Richard Baker	Derek Manas
Akila Chandrasekar	Elizabeth Murphy
Ian Currie	Rommel Ravanan
Rachel Hilton	Mick Stokes
Rachel Johnson	Gordon Turpie

In attendance:

Heather Crocombe	HC	Clinical Support Services

No.	Agenda Item	Action
1.	**Welcome and Apologies** GP welcomed everyone to today's meeting. Apologies were received as shown above.	

2.	**Declarations of Interest in relation to the Agenda** **RINTAG(21)12** There were no declarations of interest in relation to today's Agenda	
3.	**Minutes of the Research, Innovation and Novel Technologies Advisory Group Meeting held on 25 May 2021** **RINTAG(21)(M)1**	
3.1	**Accuracy of the Minutes & Action Points** **RINTAG(21)(AP)1** The Minutes of the RINTAG meeting which took place on 25 May 2021 were deemed to be a true and accurate reflection of the content of that meeting	
4.	**New study for approval: Non-Ischemic Preservation of The Donor Heart in Heart Transplantation – A Randomized, Controlled, Multicentre Trial (XVIVO)** **RINTAG(21)13** RINTAG(21)13 Study 126 XVIVO app form.pdf Please see paper for full details, but key points: • Chief Investigator – Aaron Ranasinghe (aaron.ranasinghe@uhb.nhs.uk) • Secondary contact – Stephen Clark (stephen.clark18@nhs.net) • Estimated study start date: 18.01.2021, Study end date: 31.12.2023 • UK Sites: Birmingham (Lead) and Newcastle • MHRA and IRAS approval has already been obtained • Standard heart preservation before transplantation is Ice Cold Static Storage (ICSS) for a maximum of four to six hours. This ischaemic time is directly correlated to recipient outcome. This time constraint is costly and results in severe logistical problems, leading to non-use of transplantable organs as they cannot be transplanted within the time frame • The utilisation of non-ischaemic hypothermic perfused preservation technique with Supplemented XVIVO Heart Solution (SXHS) has been shown in pre-clinical research to improve the preservation of a heart • The methodology, called non-ischaemic heart preservation (NIHP) provides a middle road between cold static preservation and normothermic perfusion of donor hearts utilising the expected benefits of both methods whilst avoiding the disadvantages • This Study is a single blinded, randomised controlled, multi-centre clinical trial, including 202 evaluable patients. The non-ischaemic heart preservation group and the ischaemic cold static storage group will be allocated in the proportions of 1:1 • The primary objective is to evaluate the effect of NIHP with XVIVO Heart Preservation devices on survival, heart allograft function, rejection episodes, and coronary endothelium preservation within 30 days, compared to standard ICSS after *de novo* heart transplantation • The secondary objective is to compare treatment groups with respect to organ function, immunological and cardiac biomarkers, graft function, serious adverse events, adverse events, major adverse cardiac transplant events, and adverse device effects • The European sites are open, and 54 patients have been randomised so far (27 to NIHP and 27 to ICSS), resulting in 48 transplants (20 NIHP and 28 ICSS). No issues have been reported for the abdominal retrieval teams. As the European sites have been running for some time, the number of patients that	

	need to be recruited in the UK may be reduced. The original UK recruitment target was 40-60 patients and now the estimate is 20-30. • The XVIVO machine is suitable for transport in an estate-type vehicle or by air. AR and team are in contact with IMT to discuss transport of the machine with them. • As the majority of heart offers will be for named patients (on the urgent list), if an offer is accepted by Birmingham or Newcastle, they will request to attend that donor (if randomised to NIHP). If the recipient is randomised to ICSS then any NORS team can retrieve the heart. • Recipients will keep their randomisation, even if that initial organ is not used for them • For hearts randomised to NIHP, the SNOD needs to request an additional three units of blood for priming the machine from the donor hospital. The team have been in contact with transfusion consultants at Birmingham and Newcastle who have devised a pro forma to maintain traceability of the blood products used. This could be emailed to the SNOD at the donor hospital on acceptance. VG queried where this pro forma would be stored and noted that there is already an MHRA-agreed process to record blood DIN numbers on HTA A forms. AR clarified that one copy of the pro forma would each go to: o The blood bank at the donor hospital o In the patient's notes o The blood bank at the recipient hospital o The research notes **AR to confirm with VG whether the DIN numbers will be captured on the HTA A form.** • Birmingham and Newcastle CT NORS teams are currently on call on the same week. If already dispatched they would like to request a delay to the retrieval to facilitate NIHP using the XVIVO machine. • If it's an off-call week for Birmingham and Newcastle, the Hub will mobilise another CT NORS team as usual. A smaller Birmingham/Newcastle team will join the retrieval; their time and transport will be funded by XVIVO. • The recipient's participation in another transplant-related study is one of the exclusion criteria for NIHP; AR is in conversation with John Dark about the impact of the SIGNET trial. In principle there is no conflict of interest but a formal agreement will be drawn up between the two studies. • There are no changes to offering or the retrieval operation itself. • DM raised that there is another potential issue with NORS teams criss-crossing across the country, because there are only ever three teams on call at once. For example, if Birmingham wanted to attend a Scotland-based donor for inclusion in their study, and the Glasgow team then had to fly to the Midlands to retrieve, this would result in increased costs. Hub Ops would have the best overview of donor activity on the night and would make the call as to whether Birmingham/Newcastle could be supported to retrieve for the study. AR clarified that the team is pragmatic about retrieving for the NIHP arm of the study. • DM also asked that the Commissioning team are involved in any discussions around transport with IMT. • MB suggested working with Julie Whitney to develop a framework for Hub Ops. • GP raised a concern around the delays to the retrieval process whilst waiting for the team to arrive, and asked AR if he had a time cut-off point in mind. AR	**AR/VG**

	advised that this would need judging on a case-by-case basis, rather than setting a strict rule, and attendees agreed. AR asked the group for approval to this Study, and there were no objections raised. ***Decision made: Attendees agreed that this is a very good study, and we should press forward with this.***	
5.	**Statistics**	
5.1	**Research Consent/Authorisation Rates** **RINTAG(21)14** Please see paper for full details, but key points: • This paper summarises how generic research consent/authorisation rates have changed over the last 10 years in the UK • Families can give generic consent/authorisation for research use of any organs which are found to be unsuitable for transplantation • Research consent/authorisation rates were analysed for actual organ donors (where at least one organ was retrieved for the purposes of transplantation) in the UK from 1 January 2012 to 31 July 2021 • When considering organ specific consent/authorisation rates, donors with contraindications for specific organs were excluded where the data is available on the UK Transplant Registry • The report shows that the overall UK consent/authorisation rate for research was 86% in 2012 and has risen to 93% in the seven months from January to July 2021. Consent/authorisation rates in 2021 so far have varied by nation from 92% in England, to 97% in Northern Ireland and Wales  RINTAG(21)14 Research consent Oct	
5.2	**Availability of Organs for Research** **RINTAG(21)15** Please see paper for full details, but key points: • This paper investigates the pathway of untransplantable organs that were offered to and received by research studies between 1 January and 31 July 2021. This includes organs that were retrieved for transplantation, deemed unsuitable and then offered for research, as well as organs that were deemed untransplantable before removal and offered through the INOAR process • Untransplantable organs data was obtained from the UK Transplant Registry for UK deceased donors between January 2012 and July 2021. Research outcome was split into three categories: (i) no generic research consent, (ii) used for research (under generic or specific consent) and (iii) organ disposed of with generic research consent • Research organ offering data was also obtained from the ODT Research Team who are copied into research offers (generic consent only). Text message offer data is manually transcribed onto a spreadsheet and combined with EOS data to determine which studies received the organs • Overall, the total number of untransplantable organs has steadily increased over time. In addition, the proportion of these organs that have consent/authorisation for research has increased to 97% for 2021 so far • The number of organs used for research fell in 2020 due to the Coronavirus pandemic. The numbers have increased again in 2021 so far – 265 organs that were retrieved for transplantation then deemed unsuitable have been used for research, and this is in line with the years prior to 2020	

	• The proportion of discarded organs where generic research consent/authorisation was obtained is substantially higher than in previous years – 13% in 2015 compared to 39% for the period January to July 2021. However, this rate is lower than the previous three years • During the period January to July 2021, 511 retrieved but untransplanted organs were offered to researchers through the National Allocation Scheme. 254 of the 511 organs offered for research were accepted by studies on the ODT Research Registry. In addition to these 254 organs, an additional 11 were used but were not offered through the NAS • Utilised research organs were distributed across many studies which suggests that studies that were ranked lower through the allocation scheme were still able to obtain research organs RINTAG(21)15 Research availability (	
6.	**New Studies and Resubmissions RINTAG(21)16(a) to (j)**	
6.1	The following studies have gone live since the last RINTAG Meeting: • **Statins for Improving Organ Outcome in Transplantation (SIGNET)** NHSBT Clinical Trials Unit and sponsored by Newcastle University • **Evaluation of the Organ Donation (Deemed Consent) Act, 2019 in England** - The London School of Hygiene and Tropical Medicine (LSHTM) • **Development of a human precision cut slice (PCS) model to study cardiac inflammation and fibrosis** - Newcastle University • The **PITHIA trial** also restarted on 1 July 2021 with the final 4 kidney transplant centres being included on 1 October 2021 • **Study 120 (rectus sheath fascia – a collaboration between NHSBT's Tissue and Eye Services R&D and Addenbrooke's NORS team** This was approved at the last RINTAG meeting and has a planned start date of 10 January 2022 **New Studies** **Study 123 – Machine Organ Perfusion of Liver and Pancreas with Real & Sensing** • This study will use a perfusion machine to keep livers and pancreases alive outside the body and will then use irreversible electroporation (IRE) on them. As most studies using IRE so far have been on animals, the aim is to better understand tissue damage caused by IRE in human tissue, making it more applicable. IRE treatment can then be made safer and more efficient **Study 125 – Evaluation of Consent Processes for Interventional Donor Research in the context of Deemed Consent** Study Aims: • To understand and evaluate the experiences and processes around informed consent for interventional donor research in the SIGNET clinical trial, from the perspective of donor families and Specialist Nurses • To identify and interpret the ways in which deemed consent may influence consent for interventional donor research in the SIGNET trial • To use the findings to make recommendations to improve the training and procedures around gaining consent for interventional donor research in the UK (setting a precedent for producing a best-practice model around consent for interventional donor research)	

Study 126
See item 4. above

Study 127 – A Phase I/II Open Label Study to assess the Safety and Efficacy of Expanded Autologous Bone Marrow (BM) derived Mesenchymal Stromal Cells (MSC) seeded onto Decellularised Allogeneic Patch of an Airway Scaffold in subjects with clinically significant Bronchopleural Fistula

- This study was presented for approval at the meeting – please see below.

Study 128 – Optimising Normothermic Perfusion of the Kidney

- To test a number of candidate modifications to a perfusion machine and associated protocol in a pre-clinical setting, with the intention of achieving a protocol and machine suitable for stable 7-day perfusion

Study 129 – Normothermic Machine Perfusion of discarded Human Livers for Development of Ischaemia Reperfusion Injury Model, and Testing of Related Therapeutic Interventions

- To develop a reproducible model of ischaemia-reperfusion injury using untransplantable human livers, and to use this model for testing anaesthetic volatile agents as interventions to ameliorate this injury

Study 130 – Risk Stratification of Renal Transplant Recipients through the identification of HLA Antibodies with Increased Risk of Antibody-Mediated Rejection

- To investigate HLA antibody-mediated rejection in renal transplant, particularly whether HLA antibodies are more likely to cause rejection than others

Resubmissions

Study 78 - Profiling of Human Hepatocytes in Health and Disease, and Generation of Patient-Specific stem cells towards Cell-Based Therapy of the Liver

- To evaluate the differences between hepatocytes isolated directly from untransplantable livers, and those generated from the same starting cells, but reprogrammed into induced Pluripotent Stem Cells (iPSCs), then converted to hepatocytes. The hepatocytes and the hepatic niche will be characterised at the single-cell-omic level, and the team will perform genomic, transcriptomic, proteomic, and metabolic profiling

Study 58 - Multiplexed Optical Molecular Imaging and Sensing during Ex-Vivo Lung Perfusion (EVLP)

This Study has three streams of work that all use untransplantable lungs on an EVLP circuit:

- Optimising technologies to characterise distal lung physiology and pathology
- Developing novel pharmacological manipulations for lungs on EVLP
- Creating a model system for segmental injury
- Concerns were raised around the number of lungs requested (200), and whether this was justifiable. This appears to be a request for an open-ended supply of organs for some years. Further justification is required for this. We should revert back to enquirer for clarity.

HT

Study 56 – Human Hepatic Progenitor Cells as a Source of Liver Regeneration

- Livers that go to this study are perfused on a machine at body temperature to assess their function. Cells called hepatic progenitors are isolated and

cultured to increase their numbers. This study then assesses whether these cells can stimulate repair in a damaged liver model

Decision made: There were no objections to any of the new studies or resubmitted studies listed above.

New study for approval:
A Phase I/II, Open Label Study to Assess the Safety and Efficacy of Expanded Autologous Bone Marrow (Bm) Derived Mesenchymal Stromal Cells (MSc) Seeded on To Decellularized Allogeneic Patch of an Airway Scaffold in Subjects with Clinically Significant Bronchopleural Fistula (also known as ENTRUST) – Videregen

- Chief Investigator: Mr Aman Coonar (aman.coonar@nhs.net)
- Secondary Contact: Steve Bloor (stevebloor@videregen.com)
- This Study is being funded by a £2.3m grant from Innovate UK
- The grant partners are Videregen (Lead), Royal Papworth Hospital (clinical partner - RPH), and the UK Cell and Gene Therapy Catapult (the Sponsor)
- A bronchopleural fistula (BPF) is an abnormal hole between the airway (bronchus or trachea) and the chest cavity. When a BPF develops, air that is breathed can travel through the abnormal hole and enter the chest cavity, which can result in life-threatening infection. BPF is a rare but potentially fatal complication of lung surgery with high death rates. It occurs particularly after removal of a lung for lung cancer or sometimes after lung transplantation
- The primary objective of this trial is to assess the safety of the tissue engineered patch at 3 months following surgery, and to determine BPF closure at 3 months post-surgery
- The secondary objective of this trial is to evaluate longer term safety, how the repair area is healing, and the subject's overall quality of life
- 5 subjects will be evaluated for this clinical trial and will undergo the implantation of the ATIMP (tracheal patch). The surgery will be performed by a thoracic surgeon who is the Chief Investigator for this clinical trial. Prior to starting the trial, each subject will undergo a two-stage screening and informed consent process.
- All of the preclinical work has been completed and the GMP manufacturing site is ready.
- LA recommended that the ENTRUST study be supported by choosing 1 ODST (either Midlands or South-East) to consent for trachea, by two different routes:

a) If lungs are allocated to Papworth for transplant, some of the donor trachea is usually discarded and could be used in the ENTRUST study
b) If lungs aren't allocated to Papworth for transplant, the research team could attend the donor hospital and remove some of the trachea at the end of retrieval for the ENTRUST study (similar principle to the olfactory bulbs project). ENTRUST already have a clinical research fellow at RPH and would need to augment this role to support this route.

- Pursuing both routes will maximise the number of cases where consent is gained and the trachea is successfully obtained for the study
- The ENTRUST team are looking for 5 samples over an 18 month period, and the trachea tissue can be banked after processing and before it's used
- The next steps are for a risk assessment and an action plan to be generated as part of a change control (managed by NHSBT). A training plan and go live date will be agreed with the operational teams.

	Decision made: RINTAG will support this study	
7.	**Ranking Working Group Feedback** **RINTAG(21)17** Please see paper for full details, but key points: • A sub-group of RINTAG was set up in 2016 to look at the fair allocation of untransplantable organs for research. Before this, organs were largely allocated on a geographical basis which was seen as inequitable, as studies that were based close to transplant centres (and particularly those that accepted more marginal organs) benefited. The current ranking system was developed with representatives of R&D, Hub Operations, NIHR, transplant surgeons and the ODT Research team. The scheme was approved by RINTAG and ODT CARE before being introduced at the same time as pager offering with a 45-minute reply time • Several concerns have been raised by researchers and other stakeholders since the scheme's introduction, which has led some studies to come up with their own arrangements (ie. they take turns being ranked first). Therefore, on 19 October 2021, a small group of these stakeholders met to discuss improvements • Feedback in general was that the scheme is overly complicated and there needs to be a mechanism for movement, ideally so that if one study has recently accepted an organ it drops down a few places to allow others a chance. It was reported that studies that are lower-ranked have to call in for research organs out of hours in order to have a chance of being allocated them - studies that are higher-ranked have the luxury of being able to accept in core hours or when it suits them HT asked for feedback from the group: • The ranking system does seem overly complicated, and it would make sense to move to a less-complex ranking model, but one which is suited to RINTAG and to Hub Operations • AFi highlighted the fact that the lung studies already rotate ranking to ensure fair allocation of organs, and this could easily be transferred across to other organs. Rather than two tiers (studies that can transplant and studies that can't) he suggested that there be a third tier of studies that are transplant-aligned. • RP advised that applications to RINTAG for untransplantable organs should ask for smaller numbers of organs and provide more (statistical) justification for why that number is required. RP also advised that studies should take more responsibility to share and allocate research organs among themselves to make best use of this valuable resource. GP agreed that this should be a priority for RINTAG going forwards and mentioned the re-instigation of the annual RINTAG stakeholders meeting to facilitate these discussions among researchers.  RINTAG(21)17 Ranking Group Updat	
8.	**INOAR Update** **RINTAG(21)18** Please see paper for full details, but key points: • In 2017 NHSBT's Research Innovation and Novel Technologies Advisory Group (RINTAG) formed a sub-group to increase the number of organs available for research. This subgroup was named INOAR	

- The INOAR project went live on 13 January 2021. Now all Specialist Nurses (SNs) in QUOD-suitable hospitals approach donor families for consent or authorisation for the removal and storage of the heart, lungs, and diabetic pancreas for research
- The data in this paper cover the period 13 January – 30 September 2021. During those 8.5 months, a total of 181 INOAR organs were offered to researchers by NHSBT's Hub Operations. The organ-specific breakdown was as follows:
    - 50% of the offers were for hearts (90)
    - 33% were for lungs (59)
    - The remaining 17% were diabetic pancreases (32)
- Extrapolating the figures for INOAR so far, and bearing in mind the ongoing impact of the COVID-19 pandemic on donation and transplantation rates, it's estimated that the first 12 months of INOAR will result in:
    - 83 lung offers
    - 127 heart offers
    - 45 diabetic pancreas offers
- Acceptance of INOAR hearts has been lower than anticipated. 90% of the offers have been for retrieval by an abdominal NORS team only, and consequently the hearts would be transported in saline. Heart researchers have advised this would make them unsuitable for their research. Several options are being considered to increase acceptance.

RINTAG(21)18
INOAR Update.pdf

Request for Specific Consent arrangements to be restarted

- A pancreas research study in Newcastle under the Blood and Transplant Research Unit (BTRU) was operating under specific consent arrangements before the introduction of INOAR. This meant that the Northern team of Specialist Nurses were taking consent from donor families for the removal of the heart, lungs and (non-diabetic) pancreas in seven hospitals in the region, specifically for the BTRU studies. Whilst the heart study has continued, the lung and pancreas specific consent arrangements were stopped in 4 of the 7 hospitals when INOAR was introduced, to reduce the impact on the organ donation process
- As INOAR only covers the removal of diabetic pancreases for research, the study team have lost a source of non-diabetic tissue for their work
- One of the aims of INOAR was to make the allocation of organs more equitable and traceable by removing local specific consent arrangements
- Will RINTAG support the request to reinstate specific consent arrangements here, and in which hospitals? If this is agreed by RINTAG, consideration should be given to other studies in the rest of the country who had their specific consent arrangements stopped, or who have been advised that they can't be supported

Points made:

1. Specific INOAR consent has been kept in some hospitals in the northern region to facilitate John Dark's study
2. BTRU (Bill Scott) is looking for non-diabetic pancreases so this would not clash with the INOAR process
3. After discussion, it was agreed that an exception can be made for Bill Scott's study (as it has been significantly disadvantaged since the introduction of

	INOAR) however we shouldn't be setting a precedent for specific consent to be reinstated	
9.	**QUOD Report RINTAG(21)19** Please see papers for full details, but key points: QUOD Bioresource Key Figures Donors 5,517 Samples 101,442 in total, including: Blood 52,223 samples Urine 12,104 samples Kidney 14,140 samples (7,163 biopsies) Liver 7,364 samples (3,700 biopsies) Ureter 8,074 samples (4,078 biopsies) Spleen 4,152 samples (4,152 biopsies) BAL 178 samples Heart 3,207 samples (1,611 biopsies) RINTAG(21)19 QUOD Statistics - Exte	
10.	**Clinical Governance Update RINTAG(21)20** There was no Clinical Governance Update available at today's meeting	
11.	**AMD Update** There was no AMD Update available at today's meeting.	
12.	**Non-transplant related research prioritisation (NODTRR) RINTAG(21)24** Please see paper for full details, but key points: • There are increasing requests from research teams focused on questions which do not directly relate to organ donation or transplantation for access to donors, families, or tissues retrieved at the time of solid organ donation. NHSBT, via RINTAG, recognised the need for an agreed policy on how such requests should be managed and facilitated • A small sub-group of RINTAG (comprising DH, RP, IC, PF, JC, GP, HT) was formed to discuss the issues and present back to RINTAG for consideration of the appropriate next step in policy development. This work was significantly delayed by the response to the COVID pandemic • Summary of topics for discussion agreed by the sub-group: (i) Scope (ii) Principles of Facilitation of NODTRR (iii) Suggested Process (iv) Unresolved Issues Attendees were asked to read and digest the content of the paper, and revert to DH with any questions or comments RINTAG(21)24 NODTRR Discussion F	

	Action: Another NODTRR sub-group to be arranged in the near future ***Action: DH to add PR and VG to the attendance list for the next sub-group meeting***	**DH** **DH**
13.	**CTU – Update RINTAG(21)21** This paper provides an update on the clinical trials in organ donation and transplantation that NHSBT Clinical Trials Unit (CTU) are currently managing. There are currently 9 trials in set-up or recruitment. A key highlight of recent activity is the SIGNET Study which has now opened to recruitment. The study will involve 80 Trusts, and SNOD teams recruiting 2600 donors over 4 years. **SONAR-12M** • Recruitment completed in June 2021. Data has been analysed, which did not support progression to Stage 2 of the Project **TWIST** • The CTU are providing administrative support to CI to open participating centres. There are currently 10 centres open to recruitment and 160 participants recruited to the trial • Recruitment is expected to continue at a positive rate with the support from participating sites **PLUS** • In set up – waiting for REC approval • Expected start date end November 2021 • Site initiation visits • Site R&D approvals pending following REC approval **DeFat** • In protocol development and set-up stage • There are 4 participating sites • All documents nearly completed for REC submission • Expected start date Jan 2022 **PLUTO** • There are 7 Trusts open to recruitment and so far, 70 patients have been randomised **PITHIA** • PITHIA was paused in March 2020 due to the Coronavirus pandemic and restarted on 01.07.2021 • A total of 205 PITHIA biopsies have been requested and processed **SIGNET** • SIGNET opened to recruitment on 14 September 2021. To date, 20 Trusts (Level 1&2 donor hospitals) have opened to recruitment, and 5 donors have been recruited to date. The remaining 58 Trusts will be opening to recruitment over the next two months **COBALT** • Protocol and study documents are being prepared for submission to the HRA/REC in November 2021 **ITOPS**	

	• The trial has completed recruitment and data collection stage, although recruitment was ended prematurely due to COVID-19, and 25 participants were randomised in total • Currently the trial team is in the process of data cleaning • Analysis will commence in January 2022	
14.	**Research Cost Recovery Update RINTAG(21)22** Please see paper for full details, but key points: • As a result of the feedback received during the stakeholder engagement event on 3rd March 2021 and to reduce any reputational risk for NHSBT whilst ensuring that the requirements of the OTDT strategy are met with regards to supporting Innovation and Research, a revised proposal for the cost recovery model for non-clinical organs was developed, this option removes the perfusion and packaging charges and introduces a set of administration fees for both the initial application for studies accessing non-clinical organs and/or tissues and an annual renewal for the studies accessing non-clinical organs • This revised cost recovery option was presented to and approved by OTDT SMT in March 2021 • The implementation of application fees for studies accessing non-clinical organs and/or tissues will go live for all *new* studies approved after 1 April 2022. Existing studies will not be affected • NHSBT Finance department will create a separate budget line for the income from non-clinical organs to assist with transparency of income. The income from the non-clinical tissues will remain within the existing budget • A communication will be sent to all stakeholders early in 2022 to ensure that they are aware of the changes and a FAQ document will be drafted and circulated RINTAG(21)22 Costs Recovery Paper.pdf	
15.	**Regional Operational Capacity Review** • There is now a two specific studies per region limit, which is the most that can be managed on top of the normal consent process already in use • The reason for the two studies limit is because of the extra training required by SNODs to become familiar with the studies they are seeking consent for • A roll out to SNODs, and training, is required with every document change, and SNODs only have a certain amount of training capacity	
16.	**SherpaPak Sharing between CT Centres RINTAG(21)23** **Request for Support of SherpaPak sharing between Transplant Units retrieved by a different NORS Team** • Static cold storage using ice boxes has been a standard practice for transporting donor hearts to recipient centres for over 50 years. Although hypothermia decelerates metabolism and the ionic constituents in the cardioplegia solution facilitate rapid cessation of electrical activity, it also activates certain processes that can ultimately be deleterious to the preserved organ. Experimental studies conducted on animal models demonstrate that almost all parts of the heart reach 0 degrees by 4 hours, between 1 to 2 hours right ventricle, interventricular septum and left ventricle all reach 0 degrees. This is also associated with electron microscopic changes	

of cellular swelling and mitochondrial calcium overload. Therefore, the current technique of myocardial preservation during transport results in unacceptably low temperature which may be detrimental to the cardiac function. The recently published ISHLT consensus document on donor heart preservation indicates that the ideal temperature for heart is between 4 and 8 degrees C

- The innovative SherpaPak (Paragonix, USA) is a CE mark and FDA approved device that has been on use in the UK since 2019, maintains the heart between 4 to 8 degrees and reduces freeze injury of the heart. The device consists of two sterile cannisters and a shipper
- The sterile inner cannister has an attachment for the aorta which is secured using a standard tie. The cannister is filled with standard NORS approved cold solution and the lid is shut tight and all air bubbles removed. This is then lowered in to second sterile cannister and is sealed tight which is then moved to the shipper. The shipper securely attaches the cannister and has LCD display of temperature and it also has a storage card for temperature measurement recordings. The cannister is surrounded by a gel pack which is stored in -20-degree freezer prior to departure for retrieval. This gel pack maintains the temperature of the donor heart and no contact of heart or the solution to the gel pack. The shipper comes with an adjustable handle and has wheels for easy transport. There is no need for any power socket, constant temperature measurement or any intervention to the heart during transport. The shipper also has a slot for samples and papers to be handed to recipient centre. It is a simple easy to use device and holds the heart in anatomical position surrounded by cold solution
- On arrival in recipient centre the co-ordinator receives the box and opens the shipper and removes the cannister from the shipper. The lid is removed allowing the surgeon to remove inner cannister in a sterile fashion and move to back table. The inner cannister is opened and the heart is removed after excising the tie holding the aorta. The co-ordinator can download the temperature data for the entire journey from the shipper
- At present this is a non-commissioned device and units are using charitable funding to purchase the device. Also, this is not part of NORS standard therefore units tend to use the box when they go out to retrieve a heart for themselves. If a centre wants to transport the heart on a Sherpa when they are not on call, then they send out a fellow with the box to the donor hospital to transport the heart retrieved by another NORS team. The additional transport cost for the fellow to attend the donor is paid by the individual centre to IMT
- **Please see Fig 1 of the paper for a Summary of Heart Transplants using SherpaPak**
- Following discussions between transplant unit directors in our meeting and also during CTAG we have agreement from all centres to start sharing the Sherpa during retrievals. This was presented in last RINTAG meeting and was supported, and a paper was requested for discussion in this meeting
- Data of all Sherpa transported hearts will be collected and will be presented during future CTAG meetings. The data on unsupervised Sherpa retrieval will be looked at specifically. Data on Sherpa versus icebox will be looked by the NHSBT statistics team and we will be able to present this data

The point was made that it was agreed at the last RINTAG meeting that a formal RINTAG application would be made for this study. LA will forward the application form to RV in order that he can complete this and submit it.

	Action: Forward RINTAG application form to RV for completion ***Action: Submit application form to RINTAG for approval*** RINTAG(21)23 SherpaPak-v1.pdf	**LA** **RV**
17.	**Any Other Business** HT has secured a secondment working with the CTU, so attendees wanted to thank Hannah for all her help and very hard work with RINTAG and to wish her all the very best in her new role.	
	Date of next meeting: 24 May 2022, from 10:30 – 15:30, by Microsoft Teams	