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A look at liver research without the medical jargon! Produced by the Centre for Liver Research, Birmingham

A leap into the future as livers are kept 'alive' outside the body

By Donna Wiles

A machine that can keep a liver 'alive' in an artificial environment is currently being tested as part of a ground-breaking clinical trial taking place in the UK.

This unique new machine, called the OrganOx $metra^{TM}$, is currently undergoing clinical trials and is the only truly portable normothermic (which means 'normal body temperature') liver preservation device available anywhere in the world. The aim of the trial is to evaluate the performance of the OrganOx *metra* in extending the length of time that a liver can be safely stored once it has been removed from a donor, and whilst in storage and en-route to its recipient.

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Normally, when a liver is removed from a donor it is stored on ice for up to 14 hours whilst being transported to its intended recipient. However, whilst `on ice' the organ gradually deteriorates as cooling only slows metabolic process but down the doesn't stop it (in the same way that meat continues to deteriorate whilst kept in the fridge). It is no longer being supplied with vital nutrients and oxvgen and its storage is in contrast to the body's natural warmth.

The crucial period of time that the organ is outside the human body and not supplied by oxygen is called the 'ischemic time'.

The deterioration of the liver during this 'ischemic time' limits the distance a donor organ can be transported within the UK, and may affect transplant success.

A further issue that may affect transplant success is the original quality of the donor liver.

Mr Hynek Mergental, Consultant Liver Transplant and Multi-Organ Retrieval Surgeon at the Queen Elizabeth Hospital Birmingham, said:

"good quality livers are declining and we are seeing more 'marginal livers'. Quite simply, a 'marginal liver' is a reduced quality liver and is mainly due to general health problems of the donor, or their age.

Ice may be fine for the storage and transit of good livers, but it can be risky for marginal ones".



Mr Hynek Mergental, one of the team at *Birmingham testing the OrganOx metra*

In this trial, once the liver has been removed from a donor, it is inspected

and prepared for transplant, then connected to the OrganOx *Metra* machine (rather than being stored on ice).

The machine then acts as a temporary host for the organ by providing both oxygen and nutrients. It also keeps it at the body's normal temperature.



The OrganOx *metra* is fully portable and is initially taken to the organ donor's hospital. Once the liver has been connected, the machine is then driven to the hospital where the potential recipient is waiting.

For the clinicians and researchers involved with the study - which is a collaboration between the Oueen Elizabeth Hospital Birmingham, University of Birmingham, Kinas College Hospital London and the University of Oxford - it is hard not to be excited as the future implications of the OrganOx metra are huge.

The crucial time frame that a liver is out of the body (the ischemic time) becomes less important as the liver could potentially be kept 'alive' for up to 24 hours. A liver could theoretically be transported all over the UK rather than being limited to a specific timesensitive retrieval and transplantation area.

More viable organs may also provide the option of more split liver transplants, thus benefitting more than one patient.

If the trial is successful, the OrganOx *metra* could mean a huge leap forward for the future of liver transplantation.

Living organ donors: a credible alternative?

The significance of the '4000th liver transplant' has recently been celebrated at the Queen Elizabeth Hospital Birmingham. The first transplant took place in 1982 by pioneering former surgeon Professor Paul McMaster, and since that time substantial advances have made transplant surgery both safer and quicker.

The problem now is the shortage of donors. Sadly, approximately 22% of patients waiting for a liver transplant will die before an organ becomes available from a deceased donor.

The increase in non-alcoholic liver disease (NAFLD) is one reason why the demand for liver transplants is on the increase. NAFLD can occur when there is a build-up of fat in the liver cells. This can normally be seen in people who are overweight and it basically means the liver has been damaged due to fat. It is known as a 'silent' disease as there are no significant symptoms until advanced liver scarring and at this point a transplant may be required.

The increasing demand for donors raises the question: **should 'living donors' be the way forward**?

Living donors can be a blood relative, spouse or friend who shares a compatible blood group with the patient, and who freely chooses to donate part of their liver.

Despite being classed as major surgery for the donor, within 6-12 weeks the liver regenerates (grows) to approximately 90% of its original size and function returns to normal.



Donors usually return to work after 6-12 weeks and full recovery for the liver takes 3-4 months but after that there is minimal impact and no life restrictions.

Before becoming a 'living donor' there is an extensive consultation process for donors to ensure they are aware of the process, implications and risks, and to help ensure the decision is the right one.

Approximately 8-10 living donor liver transplants are undertaken each year at the Queen Elizabeth Hospital Birmingham, and 25-30 per year nationally. Although this route is not suitable for all patients waiting for a transplant, it is an option which families or friends may not have previously considered, but which may be perfectly viable.

For more information email <u>Liverresearch@contacts.bham.ac.uk</u>

QUICK FACT: A liver from a deceased donor could potentially save two lives as the liver could be split so that part goes to an adult, and part goes to a child

A summer of fun for our liver education roadshow team!

University of Birmingham Community Day, 9th June 2013

On a blisteringly hot day the campus at the University of Birmingham was bustling as local families poured on site. An estimated 12,000 people attended this FREE day out which gets bigger and better each year.

The Centre for Liver Research stand was in the grand setting of the Great Hall (used for the 2010 Prime Ministerial debate and the Antiques Roadshow). Visitors took part in some intriguing new experiments designed by our scientists, learnt why the liver is vital to body health, and that liver disease has many causes. "*It's not just alcohol"* was the message our team were passing on, whilst highlighting that obesity is contributing to the increase in liver disease in the UK.



New Queen Elizabeth Hospital, Birmingham 20th May 2013

The Queen Elizabeth Hospital's annual Showcase Day highlights some of the innovative, revolutionary, novel and ground-breaking research being undertaken into a wide range of medical conditions and illnesses.

Visitors could have their health assessed for free whilst learning about the latest advances in medical treatments.

Dr Zania Stamataki takes on London!

A Virus in My Liver: Royal Society Summer Exhibition, London



The prestigious Royal Society in London was where Dr Zania Stamataki spent time in summer 2013 presenting to children and adults about the liver: how it keeps you alive, how it filters blood, how viruses '*use*' the liver and how the liver can actually heal itself!

Zania is part of the liver research public engagement team. You can view one of her Royal Society talks by visiting: http://royalsociety.org/events/2013/liver/.

Visit www.birmingham.ac.uk/clr-ppi for information on past and future events

UK-wide HCV research study: are you involved?

Chronic infection with hepatitis C virus (HCV) is a global health problem and at least 250,000 people are infected in the UK. The features of HCV infection have been intensively studied since it was discovered in 1989, however, a number of key unresolved scientific and clinical questions remain.

Through funding provided by The Medical Research Foundation (MRF), HCV Biobank Research UK was established in July 2012. This study is a consortium of leading UK clinicians and researchers who have a specific interest in HCV infection.

With support from the NIHR CLRN, this national study cohort of up to 10,000 HCV-infected people has recently expanded recruitment from 30, to 40 liver centres across the UK. A clinical research database has been established which holds records of disease progression (by questionnaires), and a biorepository holds samples from each patient recruited into the study.

At the Queen Elizabeth Hospital Birmingham (QEHB) more than 600 patients have been successfully recruited into this study which is led by Professor David Mutimer. To date, the QEHB are the second largest recruiter nationally and aims to collect specimens from at least 1,000 local HCV-positive patients.

Participation in this study involves the completion of a short questionnaire and donation of a blood sample (30-60 mls) when a patient attends hospital for a routine outpatient appointment. Processed samples are stored in the University of Birmingham's Biobank and released to researchers for use in ethically and scientifically approved research projects in or outside of the UK.

Anna Zhao is the lead research nurse on this study at the QEHB and would like to thank all patients who have participated. Email: Xiaohong.Zhao@uhb.nhs.uk

Liver disease is increasing: we need your help Have you, a family member or friend been affected by liver disease? Do you want to increase your knowledge of liver disease?

Our Patient and Public Involvement Panel is looking for new members. No prior experience or knowledge is required but an interest in liver disease is essential. This volunteer panel (the PPI panel) is run by the Centre for Liver Research Birmingham. It provides an extremely valuable contribution to our research and our studies are enhanced by the panel's involvement.

Our experts provide you with knowledge of various forms of liver disease, tell you about current clinical trials, the problems faced with trials, and discuss many other aspects relating to liver disease that few people have access to. **We give you the knowledge, you give us your thoughts.**

PPI members can live anywhere in the UK but should attend two Birminghambased meetings per year. There is an online time commitment of 12-14 hours per year. For further information contact LiverResearch@contacts.bham.ac.uk.

A National Memorial from the Donor **Family Network**

The Donor Family Network are a well-established group who support donor families and actively promote the importance of organ and tissue donation. Members are from all over the United Kingdom with some members as far afield as Poland, France, Spain, Portugal and America.

Through their tireless efforts of engaging the public over the last 16 years, it is believed that almost 100,000 new people became part of the national donor reaister.

To commemorate all organ donors, recipients, their families, and those who sadly died awaiting a transplant, The Donor Family Network are undertaking a major project for a memorial to be erected at the National Memorial Arboretum in Alrewas, near Lichfield.

The design and plans for the memorial have been approved bv the Trustees of the Arboretum and thus far, £100,000 has been donated towards the cost, but this money will only go so far.



The National Memorial Arboretum

More funds are needed to complete the purchase of the land and the maintenance for years to come, but to have such a reminder of the generosity and sacrifices of others would be a fitting and poignant permanent commemoration.

The Donor Family Network host many national events and a 'precious gift' service is held every year for recipients, donor families, medical professionals and interested parties.

Their support towards the National Transplant Games has given donor families the opportunity to present medals and awards to recipients and see how the sadness of losing a friend or family member can allow another person to live.

Visit The Donor Family Network at http://donorfamilynetwork.co.uk/. To donate towards the national memorial, or the superb work of the Network, please go to http://www.justgiving.com/donorfamilynetwork. They can also be found on Facebook and Twitter.



http://donorfamilynetwork.co.uk/



FOCUS ON: Mr Simon Bramhall

Liver Consultant at the Queen Elizabeth Hospital Birmingham

Simon Bramhall is an NHS Consultant on the Liver Unit at the Queen Elizabeth Hospital in Hepato-Pancreato-Biliary and Liver Transplant Surgery.

His main areas of clinical expertise are liver transplantation, organ donation, liver surgery, pancreatic surgery, adrenal and pancreatic neuroendocrine surgery and all aspects of biliary and gallbladder surgery.

Simon's academic interests mirror his clinical interests and he is widely published covering the majority of these areas. Simon also sits on the Department of Health Organ Donation Taskforce.

Why did you decide to become a doctor?

I decided when I was about 13 that I wanted to become a doctor, my mum was a nurse and I think I liked the thought of helping people.

How long have you been qualified?

25 years almost to the day!

Why did you decide to specialise in liver?

I liked 'big' operations and they do not come much bigger than a liver transplant!

How many years in your job did it take before you felt you truly understood the patient perspective?

1st of February 2012 when my wife became ill.

What is most gratifying about your job?

When patients get better and you think, 'I did that'!

What upsets you about your job? Surgical complications.

What is the best piece of advice a patient has ever given you? Lose weight!

Why do you think medical research is important?

Because surgeons can only do so much!

A demanding role must mean that relaxing is very important, what do you do after leaving the 'office'? When I have time I like to go walking in Cornwall with my wife Fiona, and our dog.

In hindsight, would you have chosen another career? No!

What single advancement in liver treatments <u>or</u> liver research would you like to see in your lifetime? I want somebody to grow me a liver 'to

I want somebody to grow me a liver 'to order' from stem cell research techniques.

Test your knowledge (answers at the bottom of the page)

- Should a healthy liver be:
 (a) slimy and soft, like a chicken breast, (b) hard and firm with some bumps
- How many functions does your liver perform every single day: (a) 20, (b) 50, (c) 100, (d) 250, (e) 500
- Can obesity cause liver disease and potentially the need for a liver transplant:

 (a) Yes
 (b) No
- 4. Can a liver repair itself:(a) Yes (b) No (c) Sometimes

If you would like our liver team to visit a community group, school, slimming club etc, please contact liverresearch@contacts.bham.ac.uk (apologies but we can only accept requests from Birmingham and the West Midlands).



This booklet was produced by the NIHR Birmingham Liver BRU, Centre for Liver Research, University of Birmingham and Queen Elizabeth Hospital Birmingham. Email Liverresearch@contacts.bham.ac.uk or visit www.birmingham.ac.uk/liver

Useful Contacts

Queen Elizabeth Hospital Liver Transplant Support Group: 01902 679333 (www.uhblsg.org.uk). Meetings every third Monday of the month in the QEH. British Liver Trust website: www.britishlivertrust.org.uk PSC Support Groups: www.pscsupport.org.uk/support-groups-transplant-units

Acknowledgements

The NIHR Birmingham Liver Biomedical Research Unit is a partnership between the University Hospital Birmingham NHS Foundation Trust and the University of Birmingham.

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We would like to acknowledge the Wellcome Trust Clinical Research Facility where many trials take place.



Answers to 'test your knowledge': 1=a, 2=e (500!), 3=a, 4=c (the liver is unable to repair itself if the damage is too great)