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Cambridge Intestinal Failure & Transplant

Difficult decisions: Intestinal Transplant

Dr Lisa Sharkey, Consultant Physician

Cambridge Intestinal and Multivisceral Transplant team

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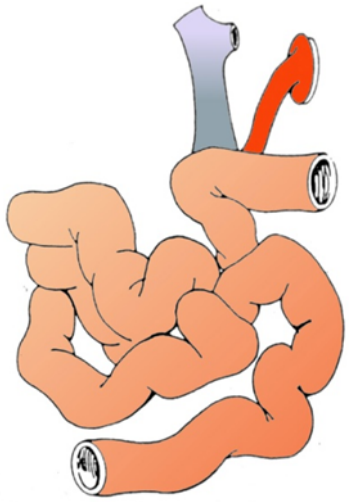
Types of intestinal containing grafts

Intestine only (SB)



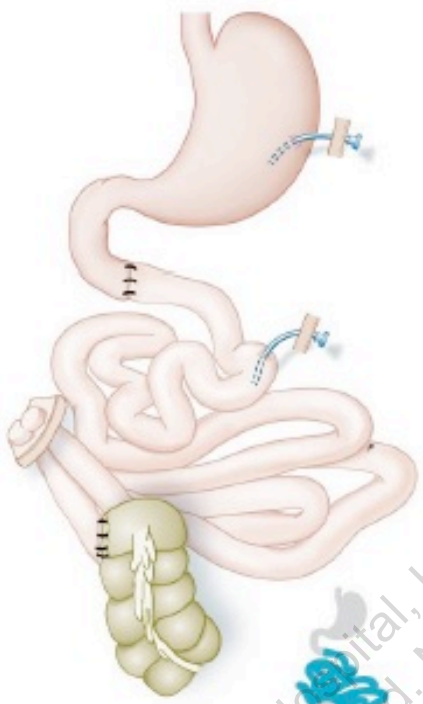
Multivisceral Transplant (MVT)

Modified Multivisceral Transplant (MMVT)

Global number of ITx = 3414

Adults / children: 49% / 51%

1964 - 2017

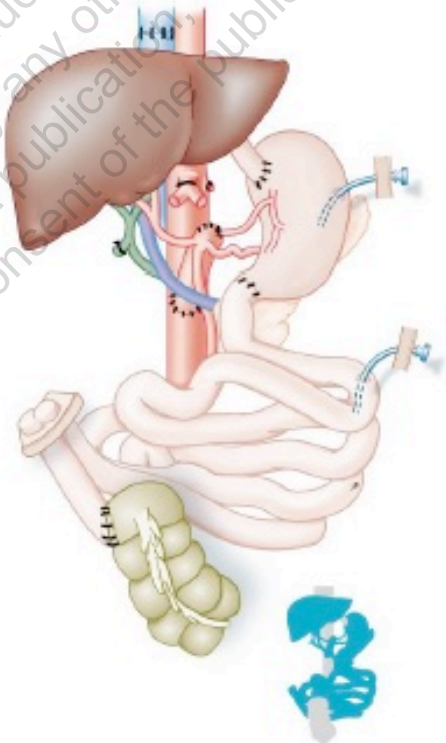


Isolated Bowel

45%

Combined Liver + Bowel

31%



Multivisceral

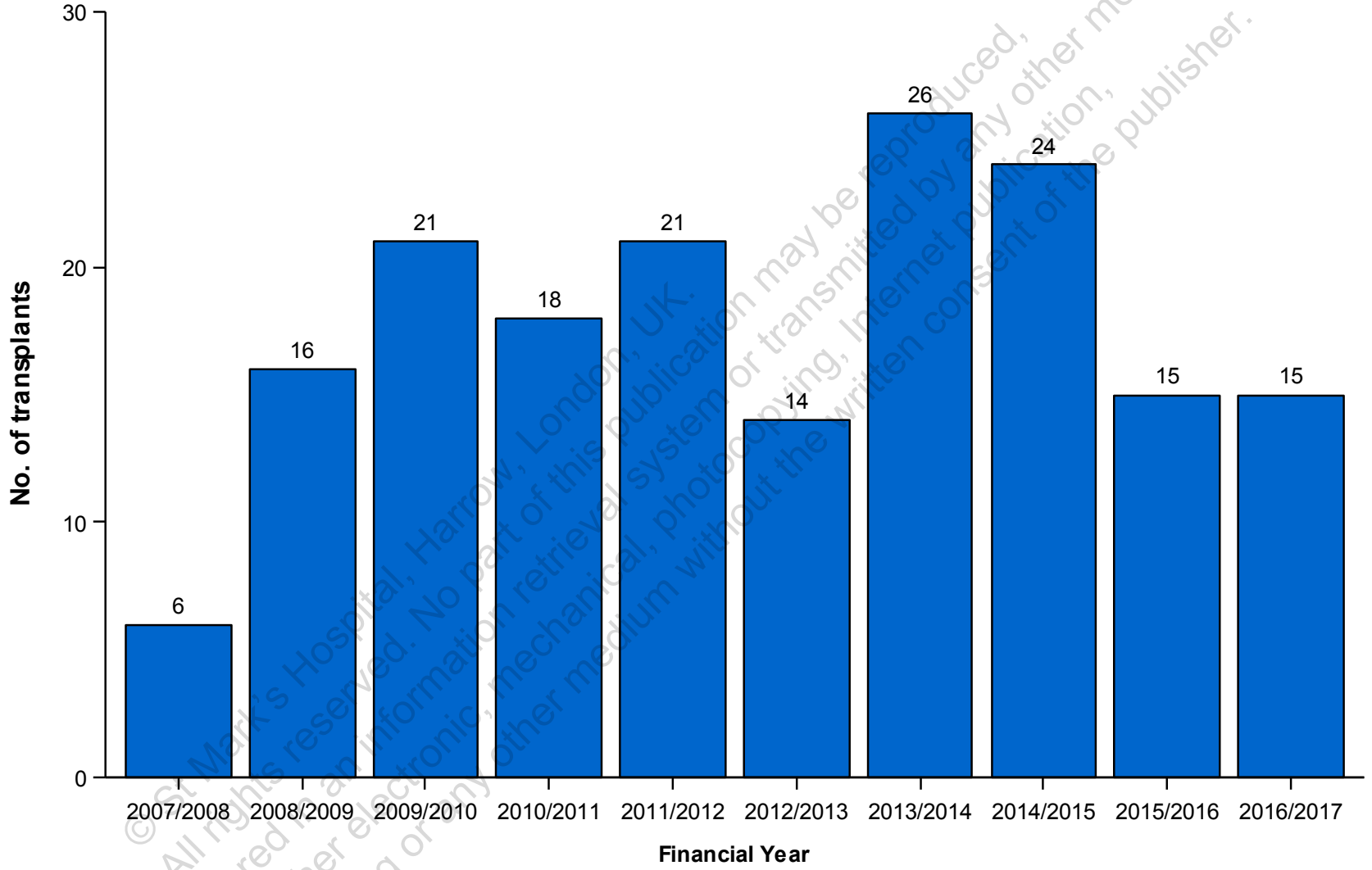
24%

Data from the International Transplant Registry presented at the CIRTA 2017, New York, USA

	LIVER	KIDNEY	HEART
UK 2016-2017 financial year	935	2159	197
US 2016 calendar year	7,496	13,431	3,190

Data from NHSBT and OPTN (deceased donors only)

Figure 2.4 Total number of intestine transplants, 1 April 2007 - 31 March 2017



Source: Annual Report on Intestine Transplantation 2016/17, NHS Blood and Transplant

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"Transplanting the bowel is crazy:
It is like transplanting a huge lymph node
enwrapped in faeces"

David Sachs

Ischemia Reperfusion Injury (IRI)

Graft-*v*-Host Disease (GvHD)

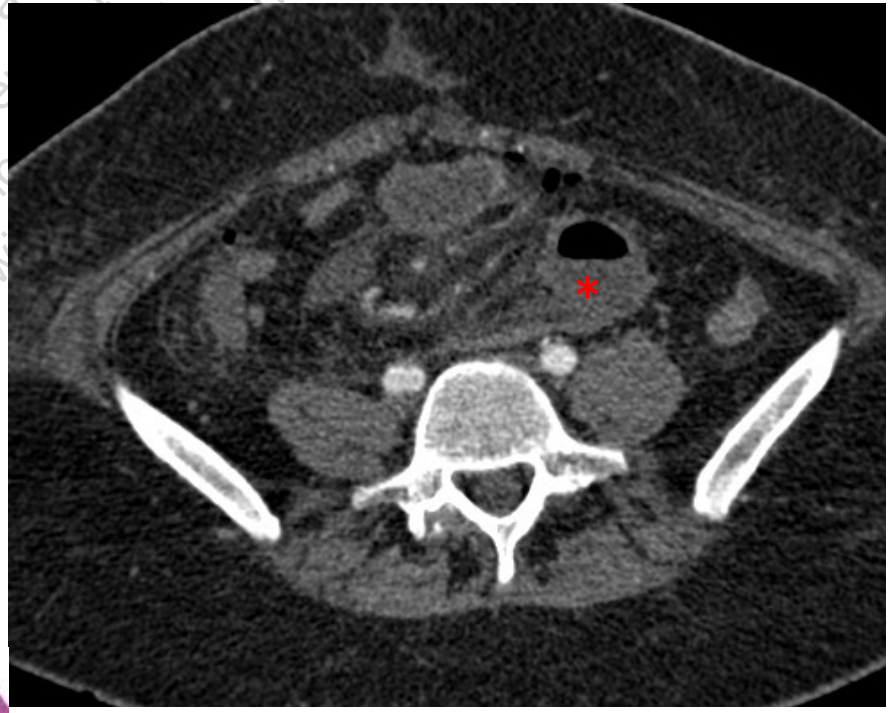
Rejection

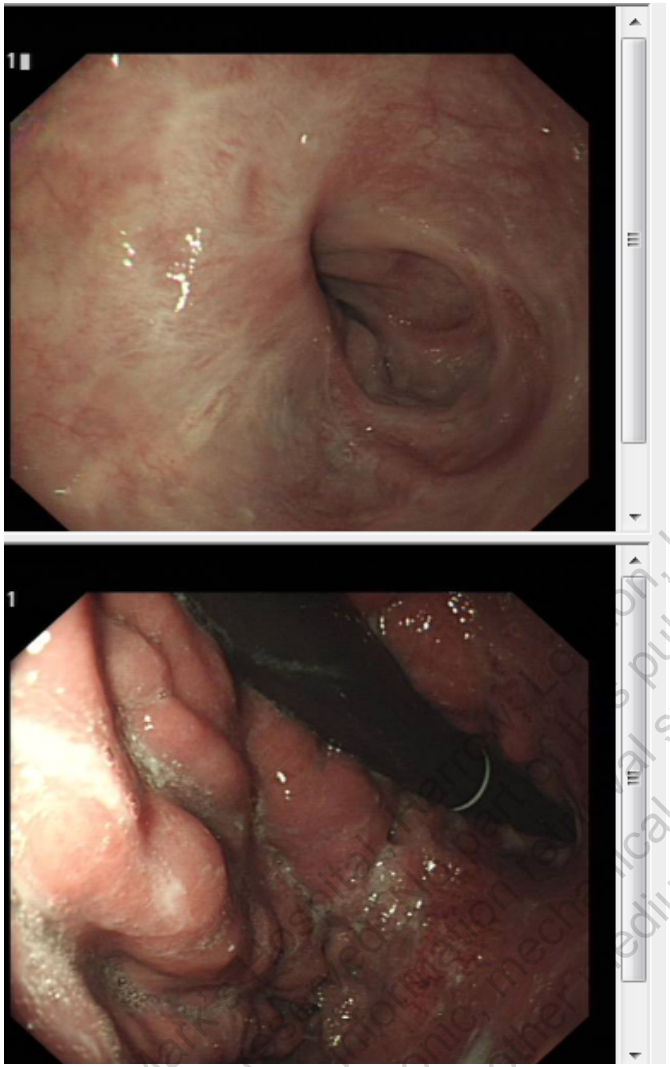
UK Criteria for Intestinal Transplant
NHSBT Patient Selection Policy Sept 2015

1. Irreversible Intestinal Failure, plus
   a. Progressive IFALD (Liver or non-liver containing graft depending on severity of disease)
   b. Severe sepsis (>1 life-threatening CRBSI for which no remedial cause can be found, or endocarditis or other metastatic infection)
   c. Limited central venous access (Venous access limited to 3 major conventional sites)
   d. Very poor QoL thought to be correctable by transplantation
2. Need for extensive evisceration, considered untenable without associated transplant
3. Requirement for transplantation of another organ where exclusion of simultaneous intestinal transplant would adversely affect survival

Emerging Indications

Widespread splanchnic ischaemia (simultaneous or sequential occlusion of Coeliac Axis and SMA)





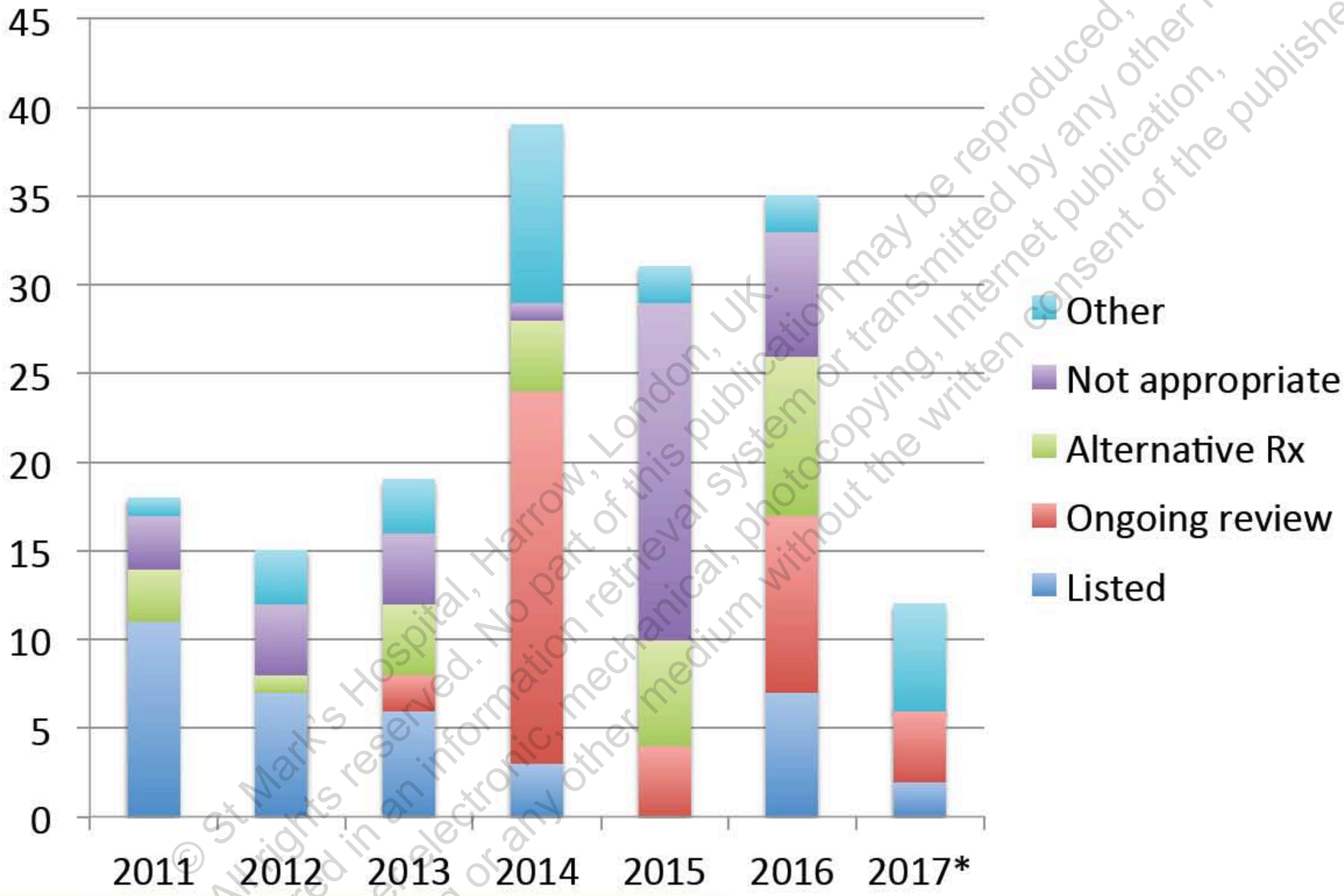
Emerging Indications

Non Cirrhotic Portal Hypertension with recurrent Life-threatening bleeding

- All other options exhausted first (TIPSS, surgical shunt, splenectomy, gastric devascularisation)

Patients requiring a Whipple's procedure with concurrent extensive portomesenteric venous thrombosis

Outcome of referrals



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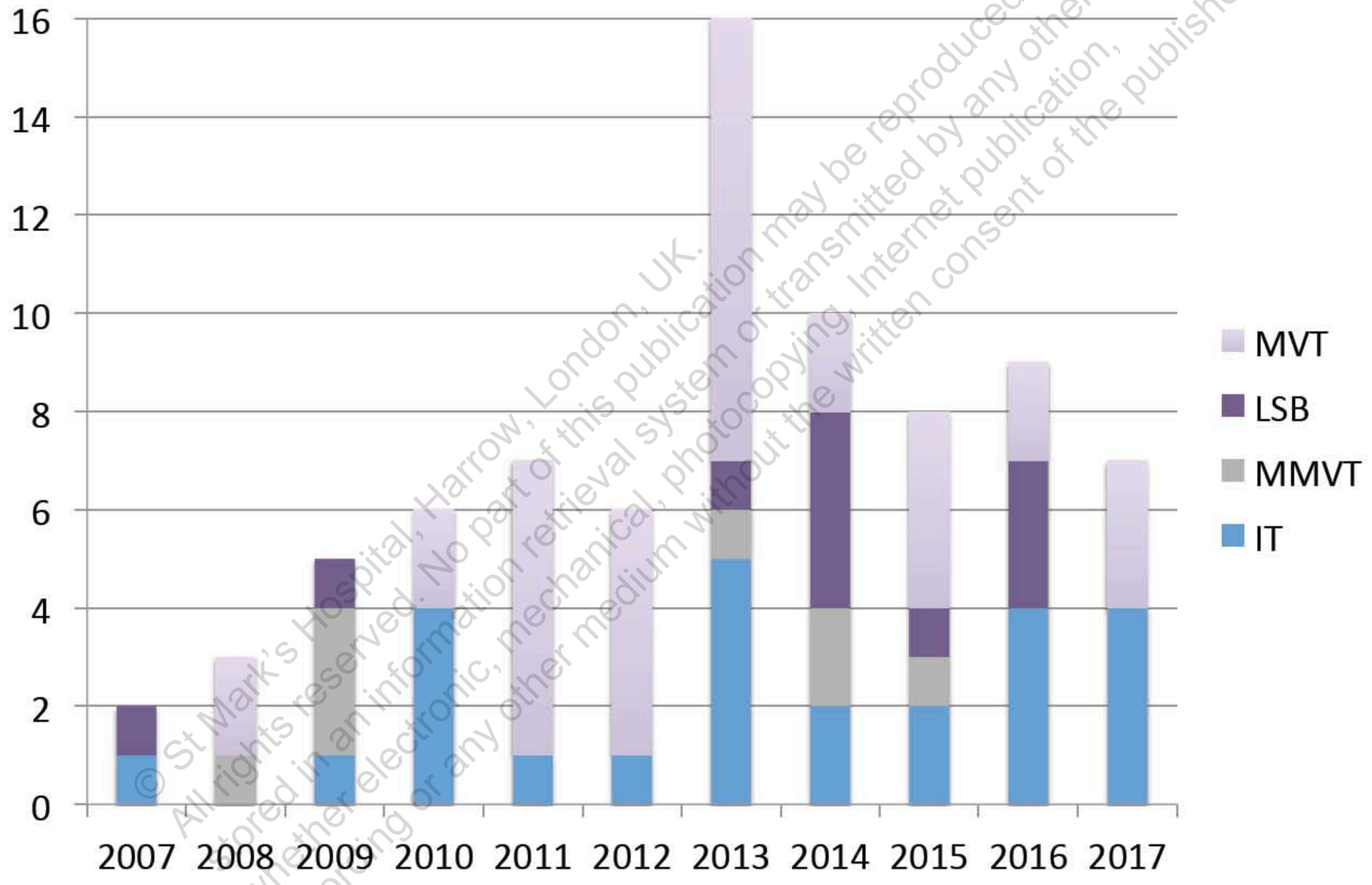
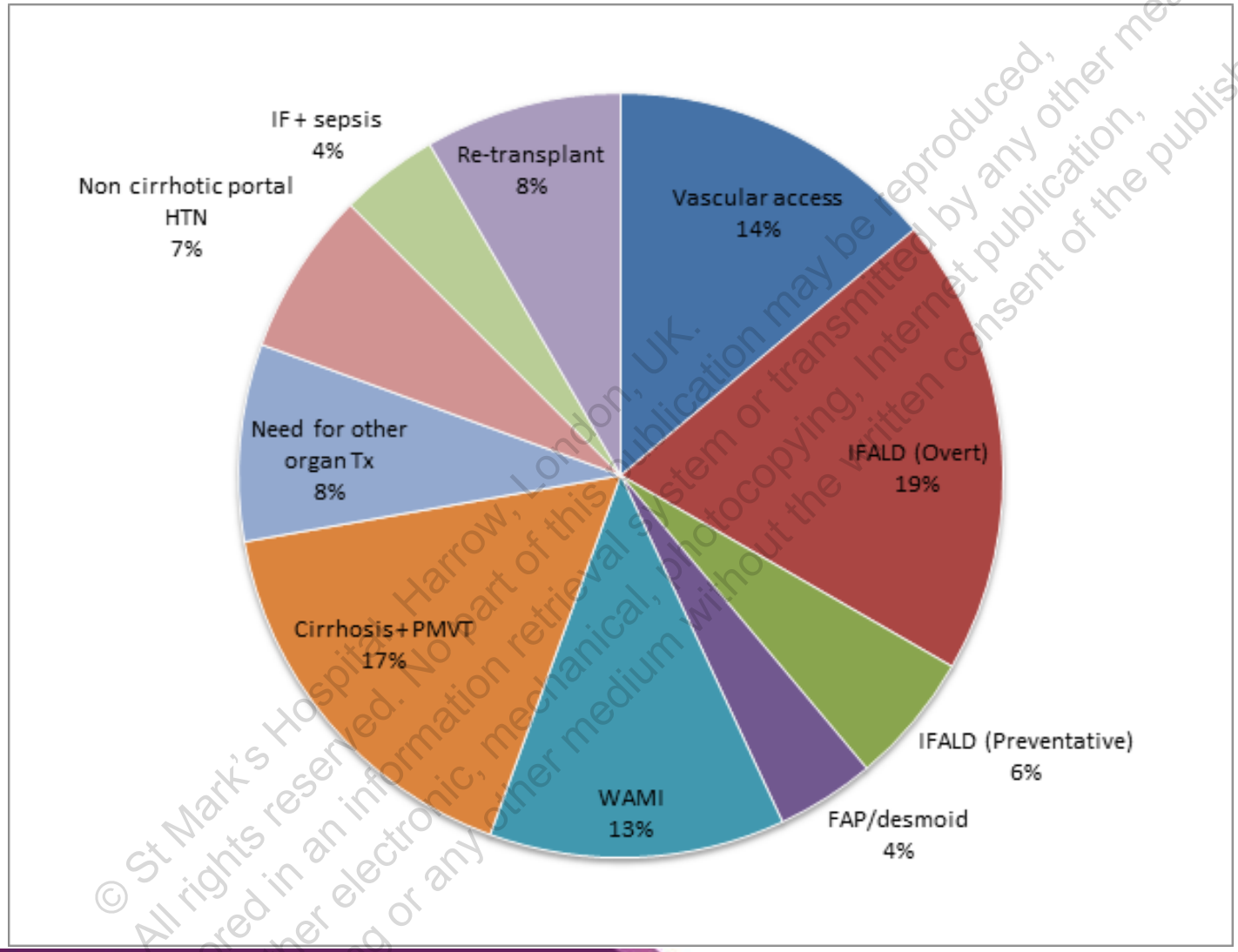
* To June 2017

Numbers transplanted by year



Indications at CUH 2007-2017



Standard assessment pathway

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Preliminary Discussion:

Adequacy of imaging

Discussion of options

Agreement on investigations

Invite for assessment

2 week assessment:

Cardiovascular

Respiratory

Radiology

Anaesthetic review

Hepatology

Nutrition

Psychiatry

Haematology

Pathology

Chronic pain

Extensive discussions re consent

Discussion at local MDT:

Multi-visceral

Liver

Renal

NASIT

Listing

The Transplant: Eviscerated abdomen

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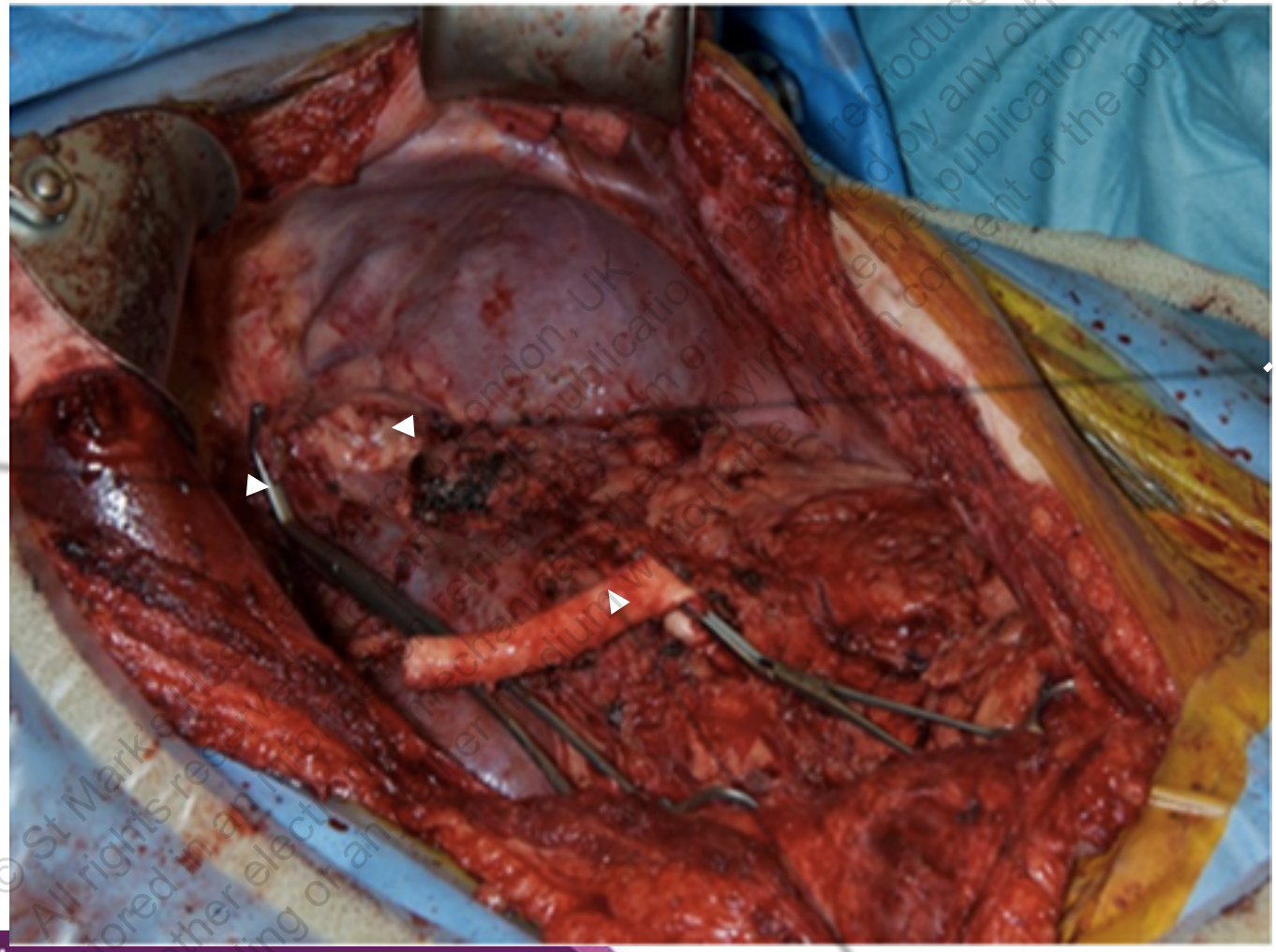

Clamp on Hepatic veins

Stapled off oesophagus

Arterial Conduit (donor thoracic aorta)

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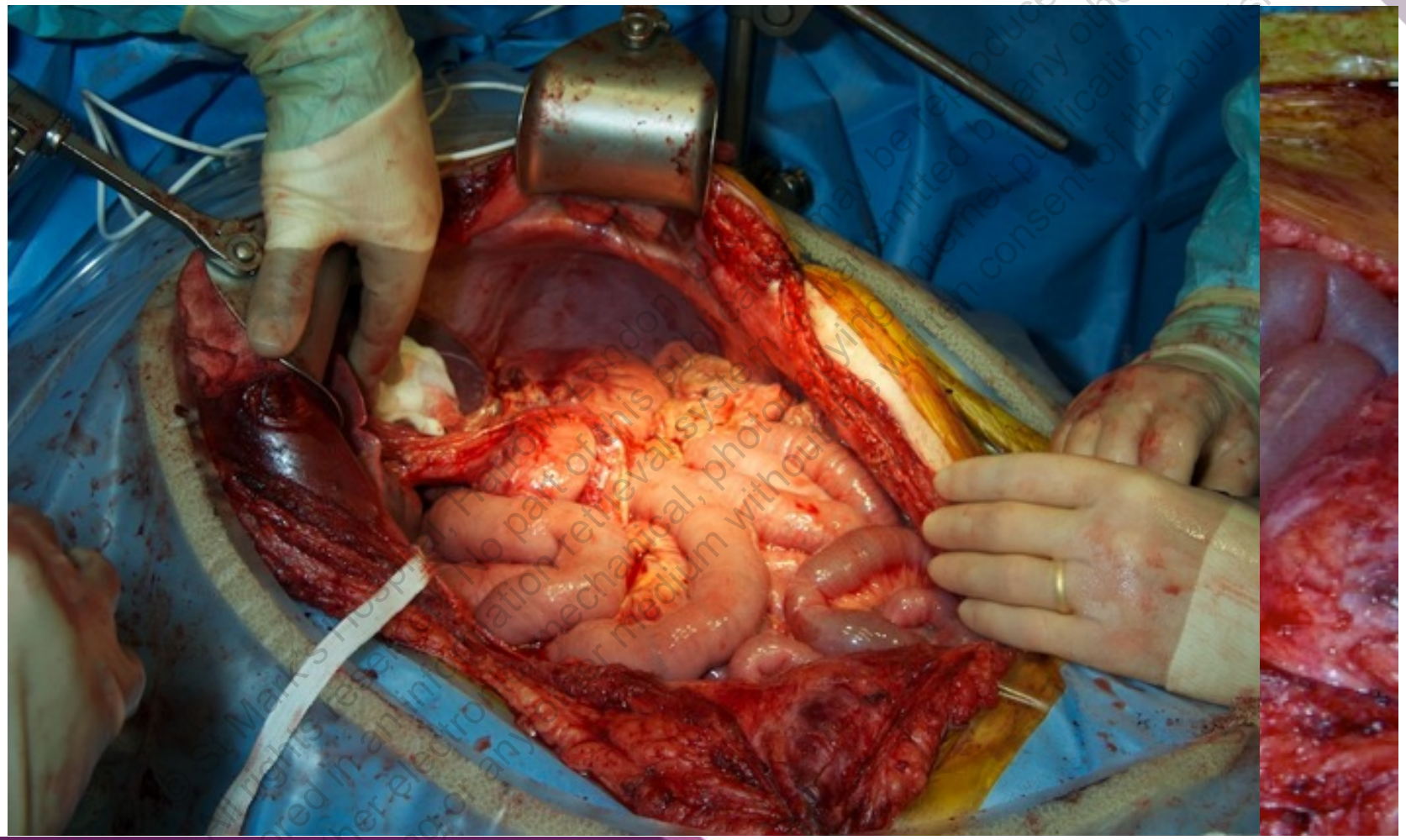
Reperfusion



Surgical problems

Time

And

Space

Immunosuppression

- Induction
  - Lymphocyte depletion (Campath / Alemtuzumab, anti-CD52) 1-2 doses
  - + Methylprednisolone 500mg
- Maintenance
  - Tacrolimus (trough level 8-12)
  - Methylprednisolone 20mg BD for first week, then taper
  - Antimetabolite from 4 weeks
- Antibiotic/Antifungal/CMV and PCP prophylaxis

Post-Transplant Complications

Not unique to Intestinal or MVT but higher rates?

- Acute cellular rejection
- Atypical (and typical!) infections
- Graft-versus-host-disease
- Coagulopathy +/- thrombotic tendencies
- Drug-induced leucopenia
- Posterior Reversible Encephalopathy Syndrome
- Post-transplant TTP
- Renal Failure
- CMV
- Encephalopathy – iatrogenic Portosystemic shunt, encephalopathy of acute rejection

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Graft Rejection

- 30-40% our patients experience an episode of acute cellular rejection (ACR) in the first year
- Presentation:
  - Asymptomatic
  - High output stoma, abdominal pain, fever
  - Severe sepsis (secondary to translocation)
- Diagnosis:
  - Graft endoscopy & biopsy – epithelial apoptosis
  - CT, US
  - Biomarkers?

Endoscopic appearances of rejection

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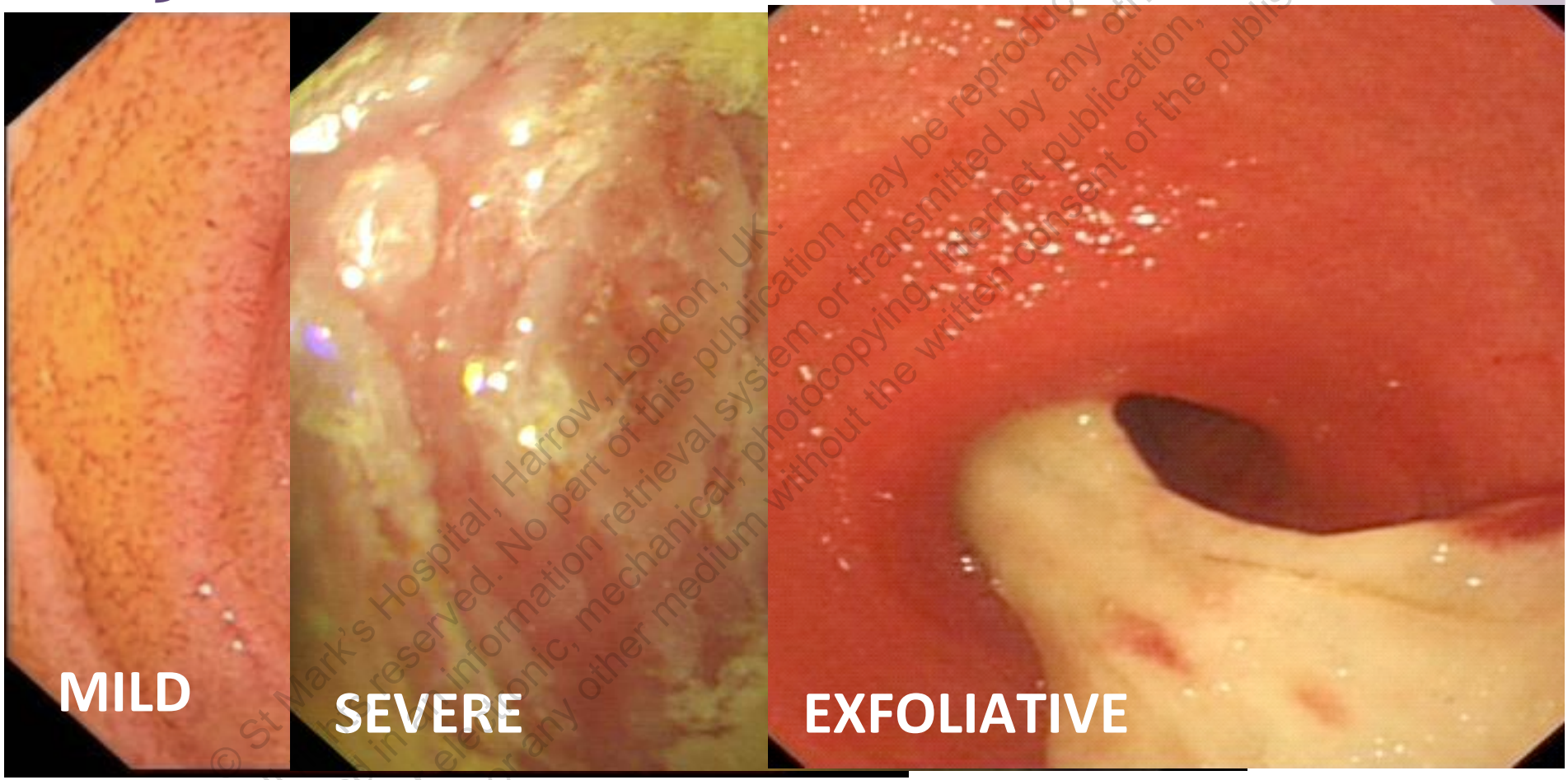

Recovery from rejection

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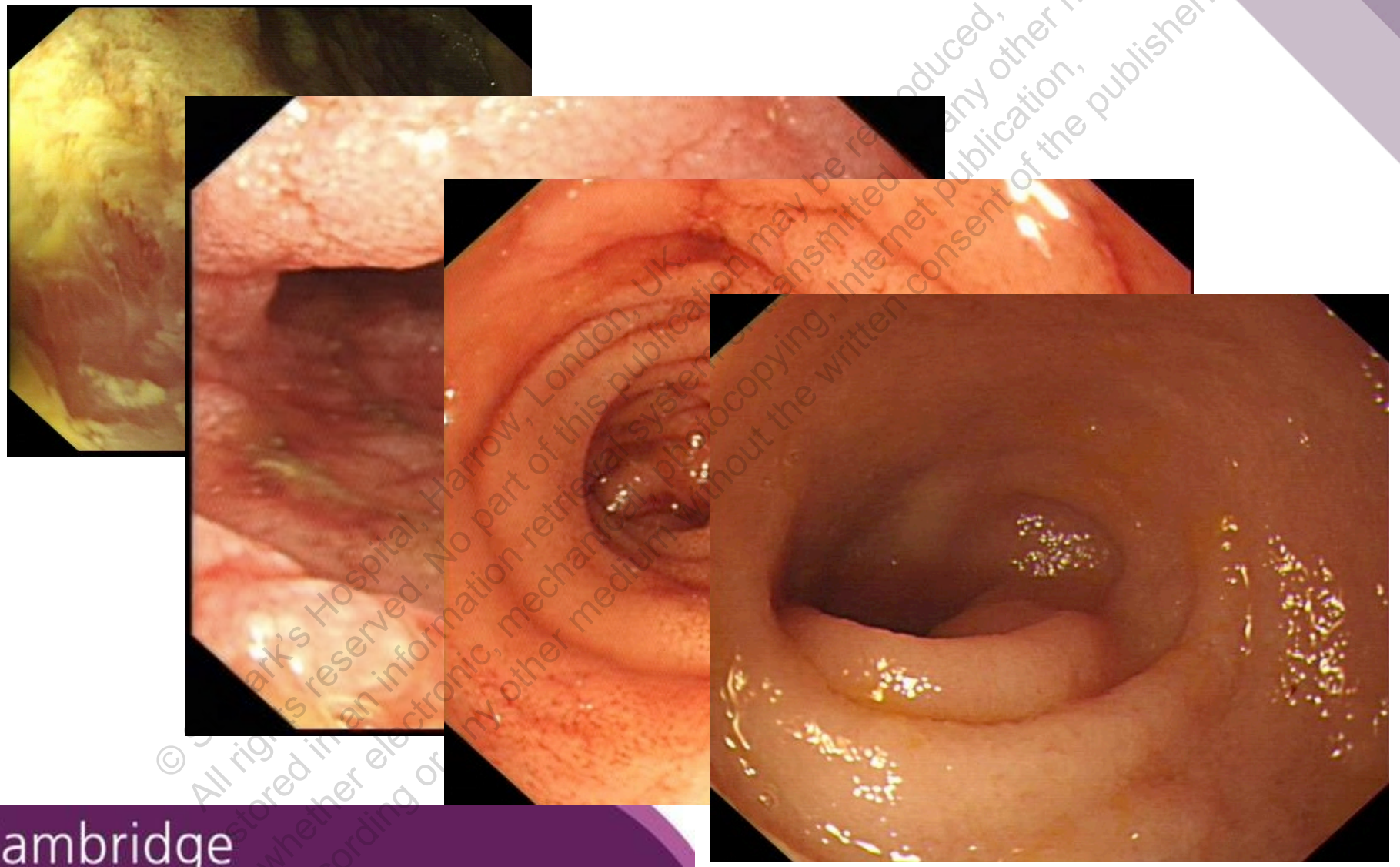

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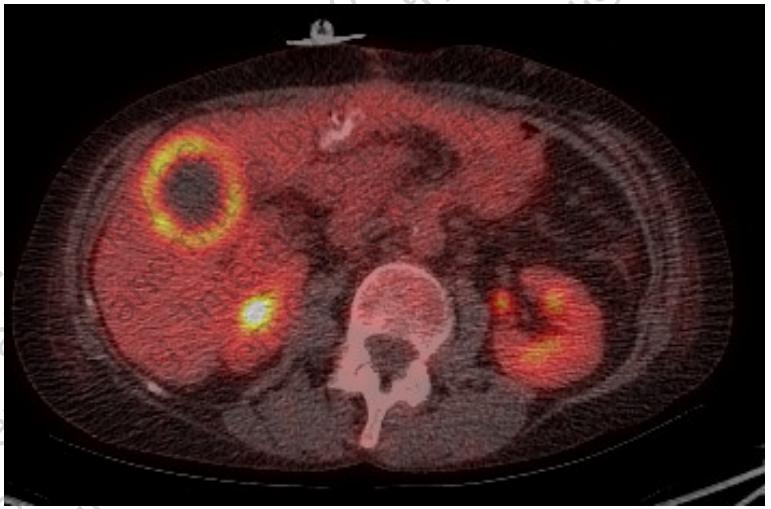
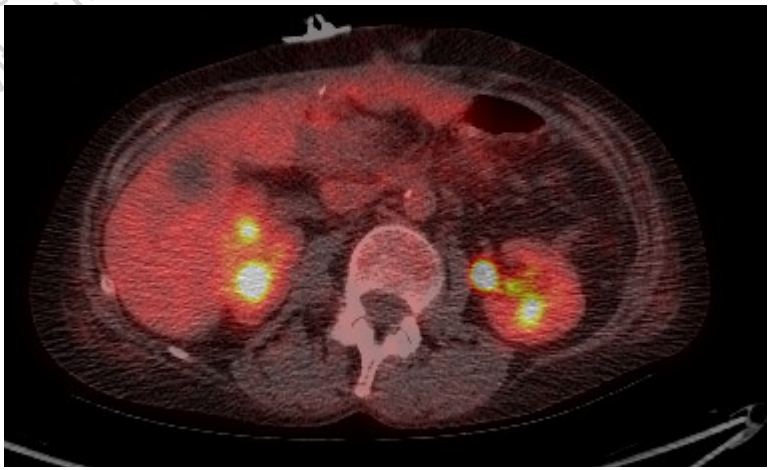
Graft versus Host Disease

- 10% incidence post ITx
- Presentation
  - Rash (biopsy-interface dermatitis, FISH)
  - Other sites – native GI tract, liver, lungs, eyes, kidney, bone marrow
  - Peripheral T cell chimerism
- Management options
  - Increase immunosuppression
  - Decrease/stop immunosuppression
  - Novel therapies

(EBV-driven) PTLD

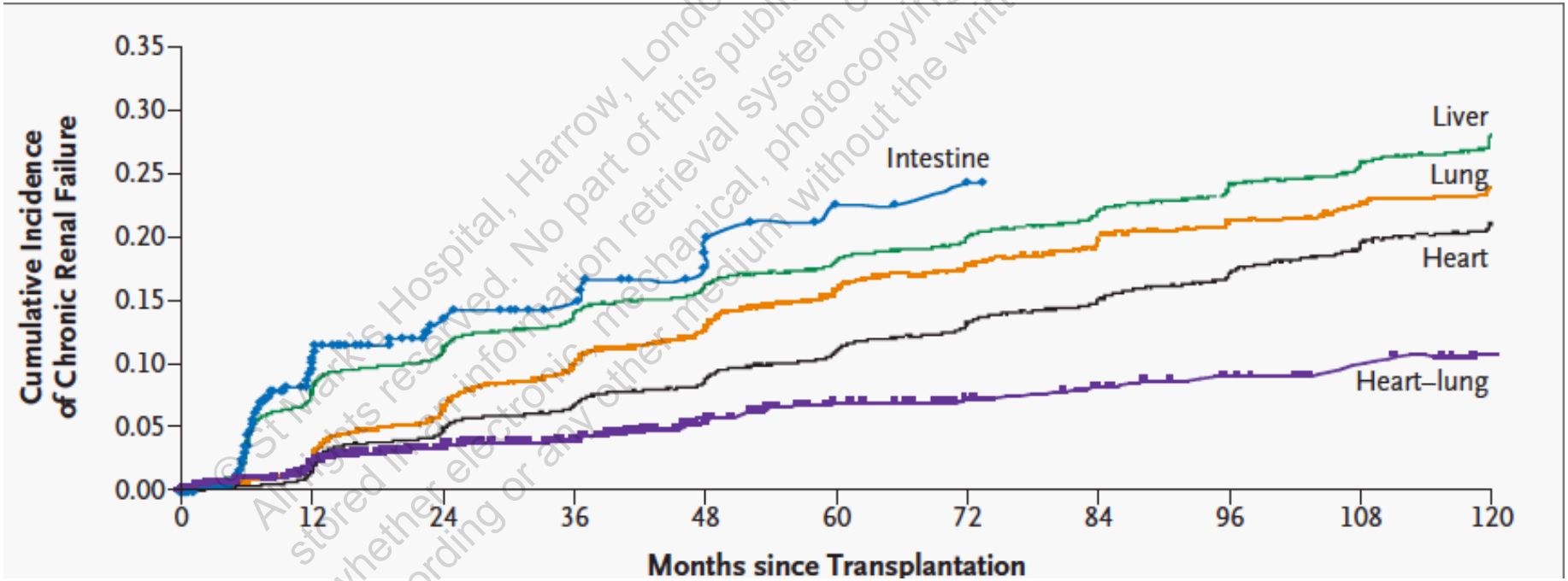
- 10%
- Treatment:
  - Reduce IS
  - Rituximab





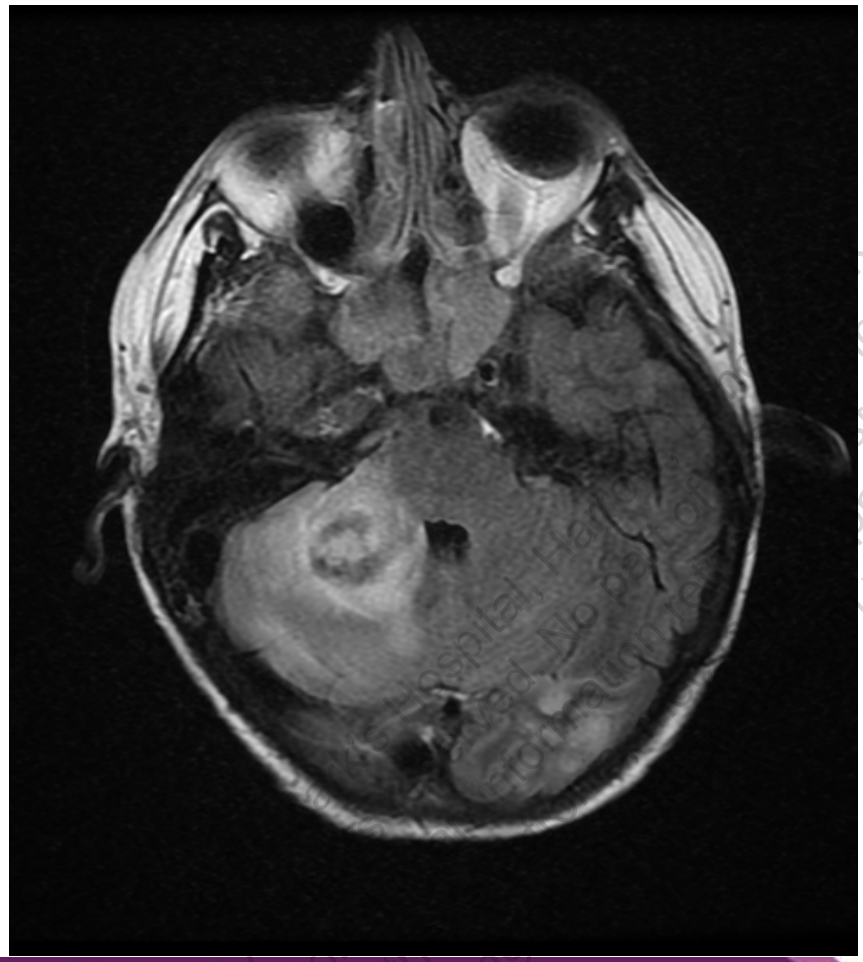
Renal Dysfunction post ITx

- More common than any other SOT
- Strategies to improve – inclusion of colon, restoring continuity, hyperhydration, switch CNI to sirolimus



Ojo et al. N Engl J Med 2011

Infections



- Increasing problem with ESBL, VRE, CRE
- Candida and aspergillus most common fungal infections
- Presence of microbiologists and infectious diseases teams at MDT crucial

RESPIRATORY MICROARRAY (BAL) (Order 43777084)

Results

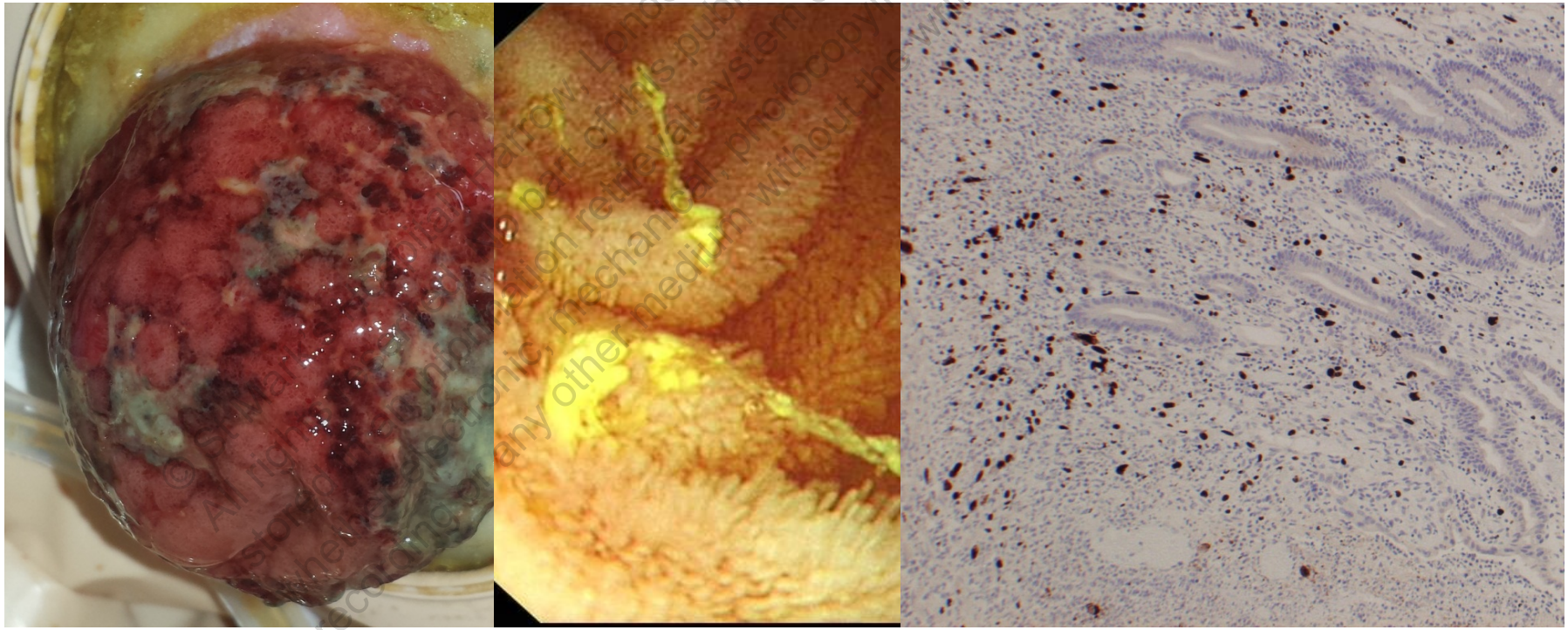
19/3/2016 08:50

Component Results

Component	Value	Ref Ra
Influenza A generic	**Detected (A)**	–
Flu A (CDC DC) CT	24	
FLU A (Q AM2) CT	23	
Influenza A H1v RNA	**Detected (A)**	–
FLU A(H12009 ABI) CT	25	
Influenza B RNA	Not detected	–
RSV RNA	Not detected	–
Parainfluenza virus RNA	Not detected	–
Human metapneumovirus RNA	Not detected	–
Adenovirus DNA, respiratory	**Detected (A)**	–
Adenovirus CT	16	
Adenovirus #2 CT	15	
Enterovirus RNA	Not detected	–
Parechovirus RNA	Not detected	–
Rhinovirus RNA	Not detected	–
Coronavirus RNA	Not detected	
Coronavirus GP-1 RNA	Not detected	–
Pneumocystis jirovecii DNA	Not detected	–
Bocavirus DNA	Not detected	–
Bordetella spp.	Not detected	–
Bordetella pertussis	Not detected	–
Legionella pneumophila	Not detected	–
Mycoplasma Pneumoniae DNA	Not detected	–
Chlamydia pneumoniae DNA	Not detected	–
Chlamydia psittaci DNA	Not detected	–
Coxiella DNA	Not detected	–
Staphylococcus aureus	Not detected	
Staphylococcus PVL Gene	Not detected	
Streptococcus pneumoniae DNA	Not detected	–
Streptococcus pyogenes	Not detected	
Haemophilus influenzae	Not detected	
Aspergillus species	**Detected (A)**	
Aspergillus 28S CT	26	

Cytomegalovirus (CMV)

- Most common viral infection
- Overall rate has fallen with matching
- GCV-resistant cases problematic



Nutritional outcomes

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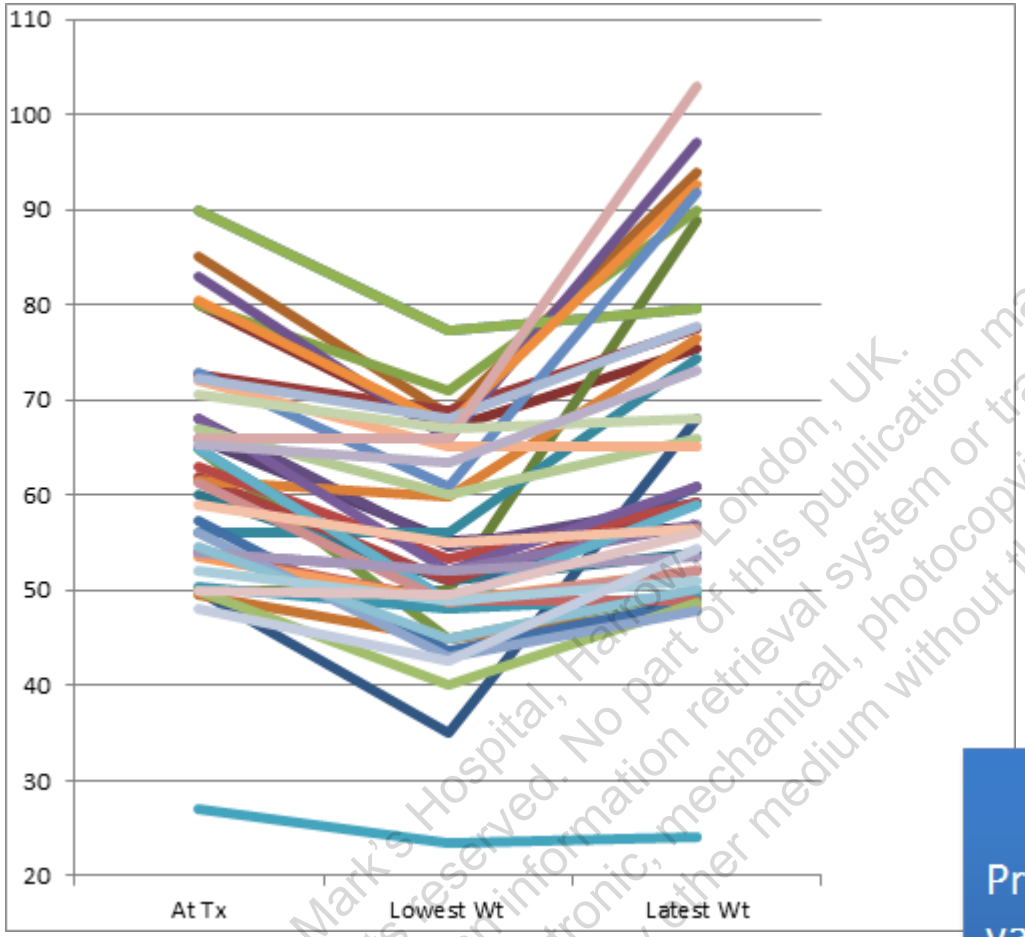

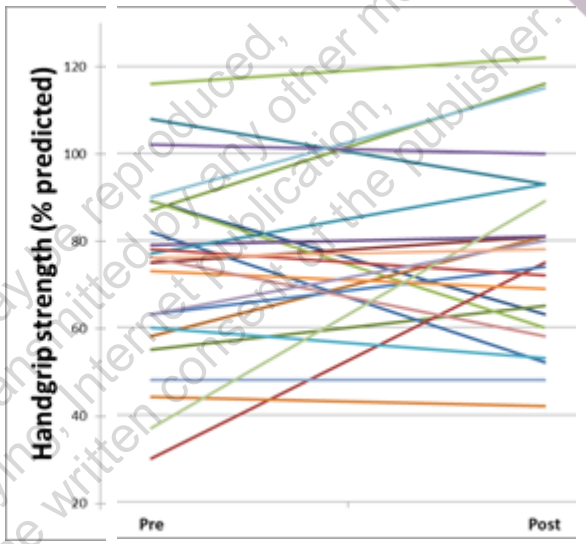

Handgrip Strength

Pre-Tx (n=38): Mean HGS 77% of expected value

Post Tx at median of 9.3 months (38): Mean HGS 73%

Post Tx at 21 months (20): Mean HGS 84%

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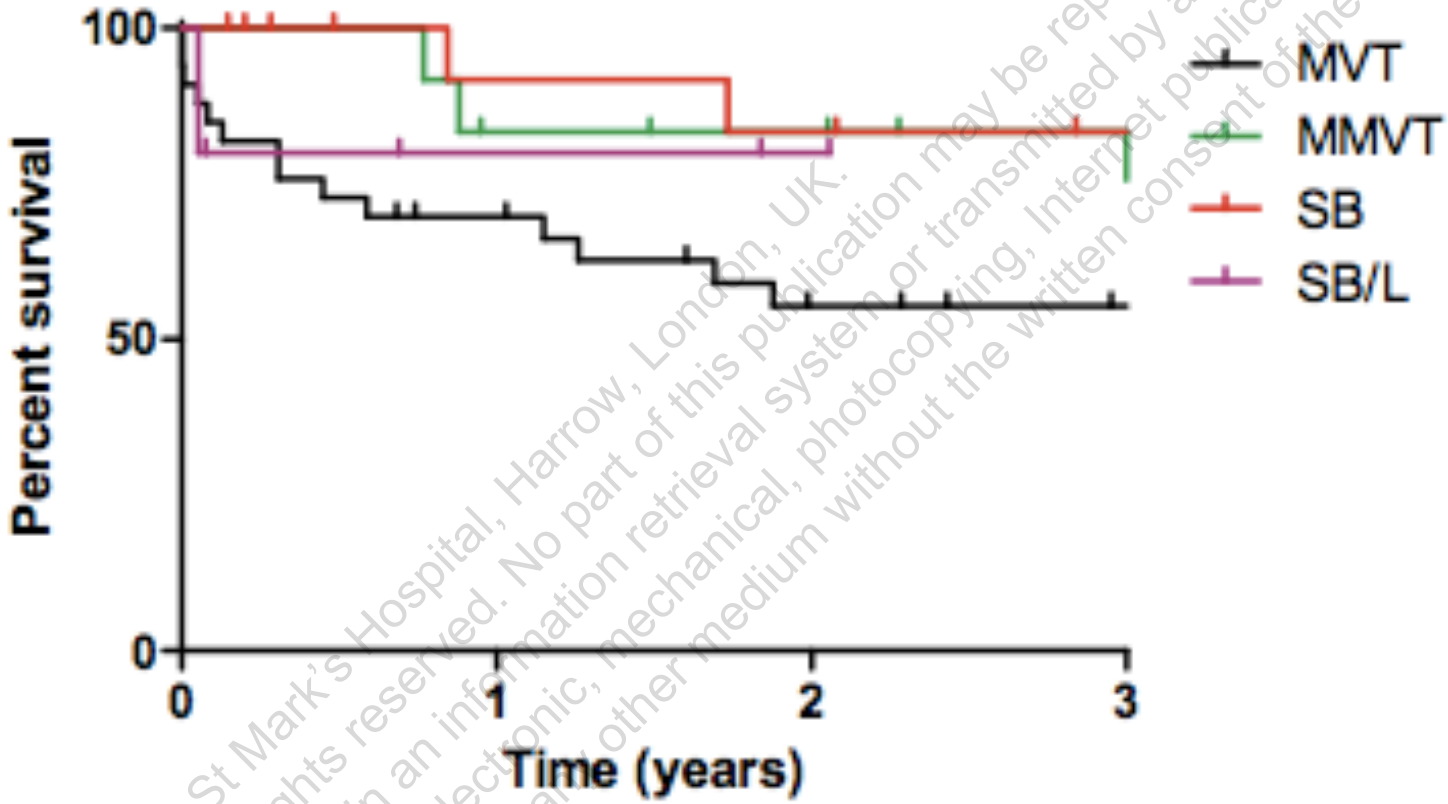
Patient **three-year survival**, **including super urgent patients**, following first intestinal transplant, by ITR group, for patients transplanted between 1 January 2006 and 31 March 2016 at Cambridge transplant unit



Intestinal Transplant in 2017

- Outcomes for Intestine-only grafts remain better than liver containing grafts
  - Esp important in IF patients (**watch the liver**!)
- Indications are expanding but other options should still be explored first
- Timely referral is key (but can be difficult!)
- Developing strategies for managing complications
- We are happy to discuss any case

Acknowledgements

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Dr David Enoch
Dr Will Gelson
Dr Jo Leithead

All fellows past and present

Our patients and their families!

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CIFT Cambridge Intestinal Failure & Transplant

Fellowships available!

- Starting March or September each year
- 6 months or 1 year
- Intestinal Failure and Transplant experience

- Email lisa.sharkey@addenbrookes.nhs.uk if you are interested