Cellutome™ Epidermal Harvesting System and ReCell™ for Vitiligo: A Randomised Controlled Clinical Trial
Declan Collins, Justin Wormald, Isabel Jones, Tony Metcalfe, Sarah Diaz

Vitiligo is a common autoimmune pigmentation disorder with a worldwide prevalence of 0.4 to 2.0 %, with greater prevalence in females and 50% onset in childhood. Conventional therapy is with topical steroids and UV light. Surgical treatment is indicated once medical therapy has failed and the disease process has stabilised. Several studies have demonstrated successful use of epidermal skin grafting using suction blisters in pigmentation disorders. Despite this, level I evidence is lacking. We propose a randomised controlled clinical trial of the Cellutome™ Epidermal Harvesting System, a minimally invasive tool for harvesting an epidermal micrograft with and without ReCell™, an autologous non-cultured cell therapy compared to conventional medical therapy for stable vitiligo.

Participants:
Adult patients >18 years old with a primary diagnosis of stable autoimmune vitiligo (not active disease)

Intervention
• Intervention 1: Cellutome™
• Intervention 2: Cellutome™ plus ReCell™

Control
• Conventional medical therapy

Outcomes (measures):
• Clinical: percentage repigmentation (digital photographs), global assessment of the disease (VAS), maintenance of repigmentation (digital photograph at follow-up), stability of disease (Vitiligo Index Disease Activity score)
• Patient related outcome measure: Skindex-29 – a validated quality of life questionnaire for skin disease, cosmetic acceptability of results (VAS)
• Basic science: melanocyte viability of Cellutome™ and Recell™ at point of graft and post healing analysis by punch biopsy to confirm established melanocyte population. (Blond McIndoe)
A randomised control trial of simple trapeziectomy for base of thumb osteoarthritis with placebo surgery arm.

Kamalathevan P, Cooper C, Vincent T, Jain A, Beard D, Gardiner MD

Oxford

Base of thumb osteoarthritis is a common cause of pain and disability. More than 3000 trapeziectomies are performed annually in the UK to treat end stage disease. The recent Cochrane review (Wajon 2015) recommended simple trapeziectomy but concluded, “We are uncertain if any surgery has benefits compared to no surgery, non-surgical therapies or sham surgery as no studies were found assessing these comparisons.” High-quality evidence to support the effectiveness of simple trapeziectomy is lacking. Published series report complication rates of 25% and continued pain in 30% patients following surgery. There is evidence that patients benefit from continued non-surgical treatment. There may be many patients having unnecessary surgery.

Population: adult patients age > 60 with pain and radiographic OA

Intervention: simple trapeziectomy

Comparators: placebo surgery, continuing non-operative management (e.g. splinting)

Primary outcome: AUSCAN 12 months
SUBMIT;Stability of Unicorticular vs Bicorticular Metacarpal Internal Fixation Trial
Bafiq Nizar, Feiran Wu, Katie Young, Rajiv Jose, Mark Foster
Institution
Birmingham Hand Centre, University Hospitals Birmingham NHS Foundation Trust.

Population
Patients presenting with an open or closed metacarpal diaphyseal fracture that require a straight plate fixation over the age of 16 are recruited and randomised into the trial from June 2015 over a period of 3 years.

Intervention
Following reduction of the fracture a unicorticular fixation is undertaken. Intra-operative fluoroscopy is used to confirm satisfactory reduction, plate and screw position.

Control
This group will have a bicorticular fixation and screened under fluoroscopy.

Outcome
The primary outcome is radiologic evidence of fracture healing at 6 month time point. Secondary outcomes measures will include, the Disabilities of the Arm, Shoulder and Hand (DASH) score, Visual analogue score (VAS) for pain movement function and satisfaction and the EQ5D. Patients are followed up at 2 week, 6 week and 6 month time points.
Randomised control trial of two versus four strand core suture repair of zone 2 flexor tendons
Bafiq Nizar, Mark Foster, Dominic Power, Rajiv Jose
Birmingham Hand Centre, University Hospitals Birmingham NHS Foundation Trust.

Population
Patients presenting with fresh (less than 7 days) open wounds to the hand with a clinical suspicion of a zone 2 flexor tendon lesion will be screened. Patients consenting to the trial will undergo further intra-operative assessment for eligibility and on confirmation of a flexor digitorum profundus, flexor digitorum superficialis or flexor policis longus tendon lesion it will be randomised to the trial.

Intervention
Following exposure of the injured tendon a two strand core suture repair will be undertaken under loupe magnification followed by an epitendinous repair. Repair technique and suture material will depend on surgeon preference. They will be splinted and referred to the hand therapist for early active mobilisation protocol.

Control
The control arm will undergo a four strand core suture repair and follow the same mobilisation regime as the intervention group.

Outcome
The primary outcome measure is the rate of tendon rupture at three month follow up appointment.
Secondary outcomes measures will include total active motion (TAM), the Disabilities of the Arm, Shoulder and Hand (DASH) score, Visual analogue Score (VAS) for pain, stiffness and function and the EQ5D. Rate of complications and re-operation rates will also be measured.
CONNECT; Collagen tube Nerve approximation versus Neurorrhaphy - Evaluation of Clinical Outcome Trial
Bafiq Nizar, Suzanne Beale, Caroline Miller, Mark Foster, Dominic Power
Birmingham Hand Centre, University Hospitals Birmingham NHS Foundation Trust.

Population
Patients presenting to the Plastic surgery / Hand surgery trauma unit with fresh (less than 5 days) open hand wounds with a clinically suspicious traumatic sensory nerve lesion will undergo pre-operative screening. Once consented, they will undergo further intra-operative assessment for eligibility. On confirmation of a complete lesion to a sensory nerve, each nerve will be randomised to be included in one arm of the trial.

Intervention
Following exposure, a collagen nerve connector of appropriate dimensions will be chosen and soaked in saline for 10 minutes. Next it will be placed over the proximal nerve stump and retracted away from the transection site. The nerve repair will be completed under the operating microscope using interrupted epineural sutures size 9-0. Following repair the nerve connector will be positioned over the suture site and secured with a single 9-0 suture at each end of the connector onto the adjacent epineurium.

Control
This nerve group will be repaired using a standard microscope assisted interrupted epineural 9-0 suture technique.

Outcome
The primary outcome is a measure of sensory recovery using static and moving two-point discrimination (tactile gnosis) using a standardised protocol.
Secondary outcomes measures will include monofilament pressure thresholds, the Disabilities of the Arm, Shoulder and Hand (DASH) score, the EQ5D, differential Tinel's sign, and visual analogue scales (VAS) for pain, cold intolerance and hyperaesthesia.
Randomised Clinical Trial Evaluating the Effect of Quilting Sutures in Length of Hospital Stay and Seroma Rate in DIEP Breast Reconstruction

Cynthia Tsang

Prolonged abdominal drainage after DIEP breast reconstruction is a common problem, resulting in patient morbidity, prolonged hospital stay and seroma formation. Quilting of the anterior abdominal wall has been effective in reducing drainage in abdominoplasty patients\textsuperscript{1,2,3,4}. The cost of suture material, additional procedural time and the learning curve required for mastery of technique may be favourably off-set by improved patient recovery, reduced length of stay and reduced rate of seroma formation requiring aspiration.

The research question is outlined below:

*For patients undergoing DIEP breast reconstruction, is quilting of the anterior abdominal wall more effective than no quilting for reducing seroma rate and length of stay?*

- **P** Patients undergoing DIEP breast reconstruction
- **I** Quilting of abdominal donor site
- **C** No quilting
- **O** Primary outcome: Abdominal drainage (total volume until removal of drains)

Length of Hospital Stay (days)
Seroma Rate (% requiring aspiration)

Secondary outcome: Complication (skin dimpling, skin necrosis, haematoma)
Patient Satisfaction

Quilting to eliminate deadspace, reducing seroma formation is widely accepted and adopted, such as in the context of Latissimus Dorsi donor site closure. However, the practice of quilting in the abdominal donor site for DIEP reconstruction is variable. A case series comparing 53 patients undergoing DIEP reconstruction showed a significant reduction in total abdominal drainage with the use of quilting (see table below)\textsuperscript{5}. There is currently no level I evidence that addresses this clinically relevant question.

<table>
<thead>
<tr>
<th></th>
<th>Total Drainage (ml)</th>
<th>Length of Stay (days)</th>
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<tbody>
<tr>
<td>Quilting</td>
<td>238.31</td>
<td>8.53</td>
</tr>
<tr>
<td>No Quilting</td>
<td>527.78</td>
<td>9.11</td>
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<tr>
<td></td>
<td>( p = 0.0005 )</td>
<td>( p = 0.401 )</td>
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The NEWS trial: Neutral vs Extended Wrist Splintage for zone I/II flexor tendon injuries
J Barnes, R Jeevan, M Gardiner, N Burr, D Kennedy, A Jain, A Iqbal

The evolution of flexor tendon rehabilitation regimes over the last 40 years has been focused on optimising the balance between immobilisation to reduce the risk of rupture and mobilisation to reduce the risk of adhesion at key times during the healing process. Timing of active and passive motion as well as splint position have been modified over the years based on surgeon and therapist experience, small scale biomechanical studies and limited, quasi-experimental, clinical data.

Wrist position has been proposed as a potentially useful variable for manipulation. An extended wrist position increases the resting level of tension across a repair while reducing the additional force needed to achieve active flexion and improving excursion. In the context of stronger 4 strand repairs replacing traditional 2 strand techniques it has been proposed that an extended wrist position may have advantages over a neutral wrist position which is most often used.

We propose a Randomised Controlled Trial investigating wrist splint position in zone I/II flexor tendon injuries.

The patient population would includes adult patients with Zone I/II flexor tendon injuries undergoing primary repair without underlying fractures or a need for revascularization.

The intervention is splintage with an extended wrist position as part of the normal therapy regime.

The control group will be splinted with a neutral wrist position with an otherwise identical rehabilitation regime.

The primary outcome measure is Total Active Motion while secondary outcome measures include rupture and adhesion rates, comfort, grip strength, patient-reported functional outcomes and activities of daily living.
Comparing Full Thickness Skin Graft Loss Rates Using Fibrin Glue versus Tie-Over Technique in Elective Skin Cancer Patients (GLUE) Trial

Theodore Pezas
Oxford University Hospitals NHS Foundation Trust

Background and Aims:
Securing full thickness skin grafts (FTSGs) has traditionally involved use of a tie-over technique whereby a bolster-type dressing is anchored to the grafted area with circumferential non-absorbable sutures. Although this is generally thought to encourage imbibition by enforcing adequate contact of the graft with the recipient site, several studies reveal that this may lead to increased tissue trauma, patient discomfort and a prolongation of surgical operating times. Use of fibrin glue to secure split thickness skin grafting has now become routine practice in burns surgery. There is currently no high-level evidence to compare use of tie-over technique to fibrin glue alone to secure full thickness skin grafts in elective skin reconstructive surgery.

Methods:
A multi-centre randomised controlled trial is proposed. The plan will be to enlist collaborators to enrol patients aged 60+ undergoing elective reconstruction using full thickness skin grafting following skin cancer (BCC and SCC) excision. Patients will be randomised to have their FTSGs tied-over or glued and then reviewed at 5, 12 and 19 days post-grafting to assess take.

Results:
Collected data will be uploaded using RedCap to ensure contemporaneous data capture. Statistical analysis will then be performed to measure primary (graft take) and secondary outcomes (patient preference, surgeon preference, operative time, cost).

Conclusions:
Deciding how to secure full thickness skin grafts following elective reconstruction post-skin cancer excision has implications for patients, surgeons and hospitals. There is currently no high quality evidence to compare tie-over technique to fibrin glue alone for securing full thickness grafts.
SIMPLIFIED PICO FORMAT

P: 60+ male and female patients undergoing FTSG reconstruction post-skin cancer (BCC or SCC) excision
I: Fibrin glue to secure graft to bed
C: Conventional tie-over technique to secure graft to bed
O: Primary: Graft take; Secondary: patient preference, surgeon preference, operative time, cost
Lopa Patel

Lipomodelling has only become technically refined and safe in the last 20 years and there is currently a paucity of long-term outcome data. Adipose derived regenerative stem cells (ADRCs) may be of therapeutic value by reducing capsular contracture rates in implant based reconstructions and giving rise to better aesthetical outcomes.

The overall demand and expectation of an aesthetically minded reconstruction has meant that increasingly breast conserving surgery is performed more frequently. In turn this has meant that lipofilling is an increasingly amenable technique to correct or reconstruct ontologically resected defects. However there is a lack of any long term patient related outcome data assessing this procedure's efficacy.

We propose a prospective multicentre UK based trial taking place over 12 to 18 months examining the effect of autologous fat transfer on patients with implant based reconstruction post radiotherapy. Participants include any women over the age of 18 up to 70 who have had radiotherapy. Half of the recruited patient population will undergo randomisation for lipofilling pre-implant insertion and the comparative standard will be implant reconstruction alone.

Primary outcome will include frequency of complications and re-procedure rate. Secondary outcomes will assess a) inpatient hospital stay period comparison for both procedures b) aesthetic evaluation of reconstruction and c) quality of life assessed via a validated questionnaire such as Breast Q assessed at 6, 12 and 18 months post procedure. A statistical comparison of these results will help delineate efficacy of lipomodelling in radiotherapy implant based reconstruction for reducing risks and improving patient outcomes.
Symptomatic neuroma may develop after a nerve dissection following any trauma to a peripheral nerve. Neuroma-induced neuropathic pain and morbidity seriously affects patient's daily life and socioeconomic functioning. The incidence of symptomatic neuromas after peripheral nerve injury is estimated to be 3-5%, however certain surgeries (autograft procedures, amputations) may have up to a 30% incidence rate.

There are several surgical procedures possible to treat symptomatic end-neuromas, but none are considered gold standard for both treatment and prevention. The most common procedure is surgical removal of the neuroma and surrounding scar tissue and placing the proximal stump into an area subjected to minimal mechanical stimulation. Unfortunately, patients with symptomatic neuromas had an average of 2.8 re-operations to treat pain and the surgeries have a failure rate of 10% or more. A resorbable poly-DL-lactide-caprolactone nerve capping device has been developed for treatment of neuromas.

By developing a conduit with a closed end (cap) it is expected that the amount of axonal sprouting is lowered due to the fact that neurotrophic hormones can not easy reach the nerve stump. Also the material is known for formation of a thin organized fibrotic layer around the cap which lowers the risk of adhesion of the nerve stump in scar tissue. A prospective European multicentre, non randomised trial has been started in which patients with primary of secondary end-neuroma of the upper limb are enrolled. Follow up will be one year and the study will be guided by MD-Clinicals.
What core outcomes should be reported in clinical research and in healthcare for patients with craniosynostosis? A systematic review, focus group and international consensus study

Thomas Edward Pidgeona, Mark-Alexander Sujanb
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Background
Craniosynostosis is a common craniofacial condition with an incidence of 1 in 1500-2000 live births. Variable outcome reporting exists within craniofacial surgery, which could potentially lead to data heterogeneity, the prevention of comparisons between studies and poor consensus on management. Variable outcome reporting can be addressed with the adoption of a Core Outcome Set (COS), but at present none exists for craniosynostosis.

Aim
Identify a core outcome set that should be reported in all future clinical research and in the healthcare of patients with craniosynostosis

Methods
This study will review the relevant literature using a Cochrane, AMSTAR and PRISMA compliant systematic review. This will summarise what outcomes are reported in studies where an intervention is used to treat craniosynostosis, and how these outcomes are defined. It will subsequently discuss these findings with clinical and lay focus groups to explore what outcomes both clinicians and the public feel are important when we treat craniosynostosis. Finally, an international online survey will be circulated to craniofacial multidisciplinary teams worldwide to identify outcomes that are most highly valued by the international craniofacial care community.

How the RSTN can help
The final step of this work requires international collaboration with craniofacial units worldwide. The Reconstructive Surgery Trials Network (RSTN) provides an ideal platform on which to develop a network of collaborating craniofacial units. In time, an independent worldwide craniofacial collaborative may form. The international adoption of an agreed COS in craniofacial surgery will unify all future clinical trials to ensure they are comparable.
Skin Preparation for Operative Trauma Of the Hand (SPOT ON)
Cobb W, Dingle L, Zarb Adami R, Rodrigues J

There are around 20122 open hand trauma episodes a year in England [2003 HES data], 97% of which require admission. Assuming postoperative infection incidence is 0.5%, 1006 infections occur annually. The cost of infections are reported as £1170-£3400/infection [Graves 2001]. Total cost of postoperative hand trauma infections may be >£3.4million. Aqueous skin preparations are commonly used to minimise surgical site infection (SSI), with chlorhexidine gluconate (CHG) or povidone-iodine (PVP-I) as active agents. NICE guideline CG74 recommends using either, and both are widely available, suggesting clinical equipoise. Uncertainty persists due to paucity and inadequacy of previous trials based on our systematic review. We propose a pragmatic multi-centre RCT:

Population
Adult patients (>16 years) with isolated open traumatic hand/forearm wounds undergoing primary surgical intervention. Patients who receive prophylactic antibiotics will be included, and a subgroup analysis performed. Clinically infected wounds (including osteomyelitis), those undergoing multi-site surgery in addition to the hand (e.g. polytrauma patients) and patients with hypersensitivity to agents will be excluded.

Intervention
Preoperative skin preparation with aqueous CHG. Wound swabs will be taken prior to surgical intervention. Randomisation will be performed in theatre immediately prior to skin preparation.

Comparator
Preoperative skin preparation using aqueous PVP-I.

Outcomes
Primary outcome will be incidence of SSI, as defined by the Centres for Disease Control and Prevention (CDC) (pus, positive wound swab, and two SSI symptoms). Secondary outcomes will include incidence and prevalence of microbial species on swabs taken intra-operatively, patient-centred complications of skin preparation including irritation, and cost utility based on the NNT.
What is the optimal time to start a dangling regime after free flap reconstruction of the lower limb

Lilli Cooper, James McGhee, Sam Orkar, Lorraine Harry and Tania Cubison
Queen Victoria Hospital, East Grinstead

It is common practice to rehabilitate free flaps using a dangling regime. However, there is no evidence to determine the optimum time to begin dangling. Current evidence suggests dangling is safe from as early as day 3 based on physiology and some clinical studies. The aim of this study would be to determine the optimal safe time to start dangling the flap after surgery.

P- Adults undergoing free flap reconstruction to the lower limb for any aetiology.

I/C- One intervention group to start dangling on day 3, the control group will start dangling on day 5 as this is common practice in the UK.

O- The primary outcomes will be flap survival and hospital length of stay. Secondary outcomes to be measured will be: complications; returns to theatre; patient satisfaction. Subgroup analysis could be performed with regards to flap type and patient comorbidities affecting wound healing.
Vivostat and ReCell for Adult Burn Split-thickness Skin Grafting: A Randomised Controlled Clinical Trial
Justin Wormald, Declan Collins, Zaid Alqalaf, Isabel Jones, Joanne Atkins

Adult burns are common and reported incidence numbers increase yearly with over 19,000 adult burns reported in 2014 in the UK. Surgical treatment is often with burn debridement and split-skin grafting (SSG) in the acute setting. A common cause of failure of SSG is graft loss secondary to haematoma, mechanical shearing and infection. Vivostat™ is a topical haemostatic agent consisting of autologous patient-derived fibrin that has been successfully utilized in pulmonary lobectomy (level I evidence), pilonidal disease and in achieving haemostasis at SSG donor sites. Vivostat™ is currently in use to aid adherence of SSGs to recipient sites and reduce haematoma formation in acute burns surgery, however the evidence for its use in this setting is minimal. Our centre currently is using this technology on recipient and donor sites for burns surgery and preliminary results are promising. We therefore propose to expand this to a randomised controlled trial of SSG and Vivostat™ with and without ReCell™, an autologous non-cultured cell therapy, versus SSG alone to establish its efficacy in terms of graft take, time to healing and cosmetic outcome.

Participants:
Adult patients >18 years old with full thickness burns requiring debridement and grafting

Intervention
- Intervention 1: SSG and Vivostat™
- Intervention 2: SSG and Vivostat™ plus ReCell™

Control
- Conventional SSG

Outcomes (measures):
- Clinical: graft take (clinical assessment), rate of haematoma (clinical assessment), days to complete healing, post-op pain (VAS)
- Patient related outcome measure: POSAS scale
- Cost analysis compared to conventional therapy
Fifth Metacarpal Base Injury Outcomes Trial
Cobb W, Dingle L, Zarb Adami R, Rodrigues J

Fracture dislocations of the hamate-fifth metacarpal joint are common injuries, often resulting from axial force along the fifth finger metacarpal typically resulting in fracture of the fifth metacarpal base with dorsal subluxation or dislocation.

Management options vary greatly between Open Reduction and Internal Fixation (ORIF), Kirschner wire (K-Wire) fixation and Conservative management. There is no established consensus on optimal management. We performed a PRISMA-P compliant systematic review of these injuries [presently unpublished], demonstrating only 4 comparative studies (level IV evidence) of management of these injuries, all with mixed conclusions, methodological flaws, and heterogeneity between studies.

As such there remains significant clinical equipoise as to best management of these injuries, and a robust randomised controlled trial is needed to resolve this uncertainty.

Hypothesis:
We anticipate that operative fixation of these injuries reduces long term pain and preserves function.

Methodology:
We propose a pragmatic multi-centre randomized controlled trial. This is likely to require a pilot study of incidence, equipoise and feasibility (with its own deliverables), with progression to full trial based on defined stop-go criteria.

Population: Full time working adults with closed fracture/dislocation injuries of the fifth metacarpal-hamate joint

Intervention: Closed reduction and K Wiring, then immobilized in plaster of paris

Control: Closed reduction and plaster of paris

Outcome: The primary outcome will be Long term hand function. Secondary outcomes will include incidence of chronic pain, stiffness, time to return to work, and patient satisfaction.