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Innovations in orthopaedic trauma: Top advancements of the past two decades and predictions for the next two☆

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ABSTRACT

The first Trauma and Orthopaedic unit dates back to 1780, originally dedicated to the treatment of children's deformities. The specialty has subsequently become multifaceted, with a plethora of subspecialty areas of which orthopaedic trauma is the most commonly practiced. Recently there has been a significant demand for an evidence base with more than 130,000 of the 162,000 publications in the last century occurring within the past 20 years. This narrative review will summarise some of the more landmark changes within orthopaedic trauma that have been made within the past 20 years, whilst also attempting to predict where the specialty will continue to develop as we move forward.

Introduction

Orthopaedic trauma is a field that sits at the forefront of orthopaedic research. Advances in receiving and resuscitating trauma patients in the accident and emergency department, implant technologies and biological therapies continue to revolutionise trauma care, affecting the day-to-day patient experience, and provides exciting avenues for future improvements in patient assessment and surgical techniques. This commentary will review some of the most important developments over the past two decades of research within orthopaedic trauma, whilst providing some insight as to the future direction of trauma research and care.

Resuscitative orthopaedics

Within the past two decades there has been significant progress made in receiving and resuscitating of trauma patients in the accident and emergency department, much of which has been led by Trauma and Orthopaedics. The provision of "damage control orthopaedics (DCO)" came to light in the 1990's from observations of the poor outcomes seen in polytrauma patients undergoing "early total care (ETC)" whereby all fractures were definitively treated on presentation as the patient was "too sick to operate" [1]. This was initially noted in multiply injured patients with fractures of the femur, in whom lower rates of complication were seen when a period of spanning external fixation was performed prior to definitive fixation despite a higher overall injury burden [2,3]. This led to the description of the second hit hypothesis, a situation in which an overactive immune system that had already been primed by trauma is further stimulated by early prolonged surgery, leading to a hyperinflammatory state that results in complications including adult respiratory distress syndrome (ARDS), sepsis and multiple organ dysfunction [4,5].

Whilst systems such as DCO provide a safe approach to the trauma patient, there exists a population of trauma patients within whom early reconstructive surgery, to facilitate early rehabilitation, is appropriate and will not lead to the complications previously mentioned. Over the past 20 years, this has been a point of focus in identifying these patients through a variety of markers including physiological observation, classification according to anatomic areas involved, and lab values that are available within the resuscitation room. Lactate has been demonstrated to be a useful marker of resuscitation and the appropriateness of early definitive surgery, with values of <2 mmol/l accepted to favour reconstructive surgery, and values of >2.5 mmol/l associated with poorer outcomes whereby a DCO approach with ongoing resuscitation is preferred [6,7]. Lactate in isolation may however be misleading,

Abbreviations: TRAUMA RESEARCH, TR; INNOVATIONS FRACTURE CARE, IFC.

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and therefore this should be interpreted in conjunction with other lab markers including base excess and coagulation, and the patients physiology. Individuals must be readily prepared to change plans should the patients condition change intra-operatively progressing towards borderline or unstable physiological states [8,9].

Alongside improvements in the science of resuscitation, both experiences within civilian and military populations over the past 20 years has reinforced the importance in the teams involved in treating these patients, including the capabilities of the receiving facility. The 2007 National Confidential Enquiry into Patient Outcome and Death (NCEPOD) “Trauma: Who Cares” report suggested that 60% of trauma patient within the United Kingdom were receiving care that was below the accepted standard [10]. This was highlighted to often occur due to a lack of appreciation as to the severity of the illness, lack of senior decision making, and inexperience in managing this patient cohort [10]. As a result, the UK Major Trauma System was launched in 2012, a method of focusing the appropriate expertise and resource on these patients which has resulted in significant improvements in the standard of UK trauma care with a 19% increase in the case mix adjusted odds of survival between 2008 and 2017 [11].

Implant technology

Further to improvements in the initial resuscitation of trauma patients, there have also been significant improvements in the technology available to trauma surgeons in treating their patients; including both technologies that are already in widespread use, and those that are showing promise within research.

Intramedullary nailing provides an effective system for treating long bone fractures with small operative scars, low rates of infection, and early return to function [12]. The earliest intra-medullary nails consisted of solid rods with cannulated nails originating in the 19th century [13]. Advances in nail technology led to the development of locked intra-medullary nails, which came into popularity during the 1970s due to difficulty in performing the procedure within multi-fragmentary fractures or those with long oblique fracture lines. This still however generally limited the procedure to diaphyseal fractures.

More recent advancements have been seen in modification in the locking options, with multidirectional screw options that allow firm hold in short segments with angular stability, expanding the potential indications of these implants to include peri-articular fractures. Nailing systems such as the Synthes Expert Tibial Nail (ETN) provide equal axial stability with significantly improved angular and torsional stability utilising fewer screws when compared to conventionally locked constructs [14,15]. Further angular stability can be achieved within these nailing systems through the design of end caps that lock onto the proximal locking screw, creating a fixed angle construct [16]. Newer designs such as the InterTan combine an interlocking lag screw with a compression screw that increases both the axial and rotation stiffness of the construct, whilst also allowing for compression of the fracture fragments further increasing stability [17,18]. Compression can also be achieved in diaphyseal fractures through the use of intramedullary compression nailing systems, which once sited can apply compression through a screw mechanism, resulting in improved bony contact and shorter times to osseous union [19]. Whilst these constructs extend the scope of intramedullary nailing, a significant problem still lies in the ageing population, and an increasing incidence of osteoporotic fractures. For this purpose, the advent of multilock nailing systems has combined the benefit of an angularly stable design with those of locking constructs in poor bone. Early results with these nailing systems in the humerus have been associated with high healing rates and excellent clinical results [20].

In addition to improvements in the design of intramedullary nailing systems, advances have been made in the preparation of the intramedullary canal to receive these devices. Reaming of the canal prior to nail insertion is performed to improve contact between the nail and the bone, and facilitate the use of larger intramedullary nails providing higher resistance to bending, axial and torsional stresses [21]. However the use of reaming is associated with an increased intramedullary pressure resulting in venous fat infiltration which can result in pulmonary complication in the form of ARDS, the risk of which is particularly high in patients already primed by trauma [22]. To try and counteract this condition, the reamer irrigator aspirator (RIA) system was created to provide concomitant irrigation within the canal and aspiration of the contents, reducing the intramedullary pressure, intravasation of emboli, and therefore the second hit [23]. In addition to its uses in preventing ongoing inflammatory response, the RIA system has also be demonstrated to be of significant value in collecting bone graft, demonstrating significantly higher yields than donor sites such as the iliac crest [24,25]. Furthermore, the system is also beneficial in the treatment of long bone infections both reducing the thermal necrosis which occurs during reaming of the medullary canal, and directly removing the infected contents post reaming [26]. Early results have been excellent utilising the technique for this indication, with low levels of recurrent infection [26].

In addition to the use of the RIA system, coated nails are becoming increasingly popular in both the prevention and treatment of bone infection. Initial nails were covered with local antiseptic substances such as silver which is able to induce cell wall disruption and therefore cell death [27]. Whilst initial concerns were made with the potential for local and systemic toxicity whilst using these implants, the implants functioned well with low complication rates and an almost three-fold reduction in infection [28]. This has been further advanced with the provision of antibiotic nails, with initial iterations consisting of custom made devices which were assembled at the time of operation consisting of Polymethyl Methacrylate (PMMA) cement mixed with a heat stable antibiotic around a threaded rod or guide wire, all contained within a cylindrical tube (thoracostomy or endotracheal tubes are often utilised for this function) [29]. The success of these implants has led to the development of formal antibiotic coated nails such as the Synthes Expert Tibial Nail PROtect [30]. These coated nails provide burst release of local antibiotics, particularly over the first 48 hours, achieving local concentrations over 1000 times that can be achieved systemically [31,32]. Antibiotic coated implants have proven useful in the management of medullary infection post fracture fixation, and are also associated with a near 75% reduction in infection rates when utilised in open fracture with significant cost benefits to hospital systems [33,34].

As with nail designs, modern day plating systems must make accountancies for the potential for poor bone quality. No more often is this met than in the management of periprosthetic fractures, where poor bone quality is often combined with difficult screw corridors, often precluding bicortical fixation, particularly with conventional locking screws. To counter this modern technology employs polyaxial plating systems whereby screws can be deployed within the freedom of a 30-degree cone. These screws initially act as cortical screws and can therefore be used to lag or facilitate fracture reduction prior to the application of locking caps which lock the screw head within the plate [35]. When utilising rigid locking fixation, one risks non-union as a result of an excessively stiff construct. This occurrence led to the development of motion lock screws which possess a smooth shaft on the near cortex, with threads engaged in the far cortex, increasing the working length of the screw [36]. The increased working length transfers small amounts of strain within the construct whilst maintain a strong hold within the bone, reducing the risk of non-union as a result of excessively rigid fixation [37]. These features provide these implants with significant flexibility, whist also maximising hold within osteoporotic bone; widening the range of indications whilst demonstrating clinical results that are non-inferior when compared to monoaxial systems [38,39,40].

Biological therapies

Non-union remains a significant challenge in modern day orthopaedics. It represents a difficult problem, that arises due to complex interactions between mechanics and biology, requiring a detailed analysis of the patient, their fixation, and the condition of the soft tissues in order to appropriately treat [41]. Even with successful treatment, patients often report ongoing pain, functional limitation, and patient reported outcome scores lower than that of the general population [42,43,44]. The diamond concept helps the treating clinician examine the components of successful fracture healing, and thereby interpret what is potentially lacking in a non-union scenario [45]. This concept suggests that for successful fracture healing to take place, the local environment requires the presence of osteogenic cells, osteoinductive mediators, an osteoconductive matrix, appropriate mechanical stability, and an adequate blood supply [45].

Mesenchymal stem cells (MSCs) are the osteogenic cells involved in bone healing. Within non-union tissue, MSCs have been demonstrated to become impaired with reduced osteogenicity, and therefore augmentation with MSCs is frequently required in the surgical plan when dealing with non-union [46,47]. This may be in the form of processed bone marrow stromal cells (BMSC), or more commonly minimally modified bone marrow aspirate concentrate (BMAC) which can be prepared intra-operatively and contains additional growth factors that promote MSC proliferation and differentiation [48]. Whilst there are no randomised or comparative studies, the augmentation of non-union with MSCs in the form of both BMSC and BMAC has been associated with high rates of union and good clinical outcomes [49,48].

Critical to the proliferation and differentiation of MSCs, is the signalling within the local environment, particularly the presence of growth factors including platelet derived growth factor (PDGF), fibroblast growth factor (FGF), insulin like growth factor (IGF), and the transforming growth factor beta (TGFβ) family of proteins including the bone morphogenic proteins (BMP)-2, 4, 6 and 7 [50]. These osteoconductive factors can be delivered through the use of platelet rich plasma (PRP) taken at the time of operation and either directly injected into the non-union site or mixed with bone graft if a larger defect is being treated. These techniques have been demonstrated to result in excellent rates of union with shorted healing times when compared to fixation alone [51,52]. BMP-2 and BMP-7 have also gained popularity in augmenting MSCs when treating non-union, utilised in their role of osteoinductive mediators. The use of BMPs has been demonstrated to achieve union rates in excess of 90% in tibial non-union, and interestingly have also been demonstrated to result in increased expression of angiogenic mediators potentially suggesting that their beneficial effect is not just limited to osteoinductivity [53,54]. Their use in the treatment of grade three open tibial fractures has also been demonstrated to be efficacious, with fewer reinterventions required to achieved union and significant cost benefits to the health system treating these patients [55]. Further research has demonstrated their potential interest in other long bones including the femur, tibia and humerus; demonstrating faster healing times with their use [55]. That being said these molecules still remain novel, and require further research with comparative trials before their true impact, indications and role can be agreed.

Bone healing and regeneration becomes significantly more difficult when critical sized bone defects exist, be that due to bone loss at the time of injury, or bone loss as a result of debridement of the devitalised segment. In this situation an osteoconductive matrix must be provided, in addition to the osteogenic and osteoinductive elements. Bone void fillers such as CERAMENT (BONE SUPPORT AB, Ideon Science Park, Sweden) provide useful adjunct when structural graft is not required [56]. These biodegradable calcium based synthetic materials provide an excellent osteoconductive scaffold for the migration of MSCs, promote ingrowth of blood vessels, and can stimulate new bone formation at a rate similar to autogenous bone [57], [58]. Furthermore these products have the advantage of being able to provide local antibiotics to the defect in situations where infection is either known or suspected [59].

Another group of popularised non-structural scaffolds are the collagen-based scaffolds which also demonstrate excellent biocompatibility, osteoconductivity, and osteoinductivity. Their structure can be modified to adjust pore size in order to facilitate both bone and vascular ingrowth, and they can be combined with polymer to improve their mechanical properties [60]. These sponges can also be laden with antibiotics therefore expanding their use to cases of bone infection. As a material that subsequently biodegrades, they offer significant advantage over other local antibiotic carriers, such as PMMA, which require a second procedure remove. Furthermore they have also been demonstrated to facilitate bone healing even following infection, meaning that further surgery to treat the bone defect is not required [61,62]. The literature is still however low quality with regards to these devices, and further comparative studies are required.

Future directions

Whilst the rate of discovery within the field of orthopaedic trauma increases, further questions continue to arise and the specialty must keep pace in order to drive clinical care forward. Future research will likely build upon those topics already discussed within this commentary, whilst also moving towards the provision of more individualised care with the treatment of each patient based upon their individual susceptibility and recovery potential.

Increasingly it is becoming clear that each individual has a different genetic preponderance to a disordered inflammatory response following trauma, and therefore whilst total injury burden and physiology may be identical in two individuals, one may be appropriate for EAC, whilst the other may come to serious harm if this approach is adopted [63]. This abnormal response to trauma most commonly occurs as a result of single gene polymorphisms, with the most significant being in the allele coding for IL-6 [64,65]. Whilst a timely and useful bedside test is not yet available, techniques such as multiplex cartridge-based PCR have grown to popularity, particularly within prosthetic joint infection, allowing the identification of numerous DNA sequences present in a sample within 3-4 hours [66]. Once available, a bedside test highlighting each patient's genetic preponderance towards their potential immune dysregulation could be of significant benefit when deciding on adopting a DCO vs Early Appropriate Care (EAC) approach. Furthermore, advances within genetic testing such as whole genome analysis and next generation sequencing may raise light on further locus that could shed light on other susceptibility genes, and potentially provide targets for directed therapies [67].

Further advances are likely also to be made in monitoring fracture healing in patients undergoing fixation through the use smart implants. Devices have already been created that can be implanted either within the fixation device or directly at the fracture site, and can provide information regarding strain and impedance, both of which can be interpreted in a manner to reflect stages of fracture healing [68,69,70]. Whilst development within the field is still relatively young, the potential for the technology may prove revolutionary within the field of trauma surgery. Over time smart implants will provide large-scale real-time monitoring of fracture healing, with the development of normograms stratified by age, site of injury, and comorbidities that affect bone healing. This will facilitate the identification of early complications, with the possibility of early intervention for patients who fall off the treatment normogram whilst the biology of the fracture site remains more amenable to intervention. Furthermore this will reduce the requirement for routine radiographs reducing the overall radiation dose to the patient whilst also opening up increased opportunity for remote follow-up pathways providing both benefit to the patient and reduced system costs [71].

An increase in 3D printing is likely to continue within the field of orthopaedic trauma in order to support the routine management of fractures alongside the treatment of complications. 3D printing already has a number of applications including the printing of anatomic pre-bent plates, pre-operative planning through the printing of customised fracture models, advanced templating in the treatment of post-traumatic deformity, and in training based on in-vitro fixation of the fractures of real patients [72]. This technology can also be utilised in the treatment of bone defects through the custom printing of biodegradable scaffolds which are gradually replaced over time with native bone [73]. These are commonly ceramic materials such as bioactive glass or hydroxyapatite, often combined with polymers such as polylactic acid (PLA) to counteract their brittle properties [74]. Despite efforts to improve their mechanical properties, these materials remain poorly tolerant to loading, and therefore alternates continue to be pursued [75].

In further attempts to pursue autologous solutions to bone defects, efforts are turning to techniques to support and contain autologous bone graft with devices such as the TRUMATCH [76]. Each cage is custom printed to fit the patient defect, with a central core and open outer face design to allow revascularisation of the segment without central necrosis. Animal data has demonstrated greater graft retention when compared to membrane based alternatives, a return to near normal torsional strength at 18 weeks following a 3cm segmental defect, and an accelerated transition from woven to cortical bone [77]. Whilst still at an early phase, this device appears an exciting prospect and we eagerly await further data.

Bioprinting similarly presents a potentially exciting avenue of research regarding management of bone defects. This technology allows the production of an exact biological structure consisting of cells and extracellular matrix components, with in built vascular channels. This potentially avoids the problems observed with other 3d scaffolds, which are dependent on cell and vessel ingrowth in order to achieve bone regeneration [74,78]. In addition to the potential clinical applications, creation of ex-vivo models will also allow further study of disease processes such as non-union whereby the investigator can manipulate the local environment (such as the ECM), adjust the local cytokine environment (such as growth factors), and manipulate the mechanical environment that the tissue is exposed to. This will facilitate evaluation of MSC behaviour in response to a changing environment, potentially leading to a better understanding of non-union and identification of novel treatment strategies.

Conclusion

Research within the field of orthopaedic trauma has advanced significantly over the past two decades, with advances seen across the spectrum of resuscitation, engineering, and cell therapies. We anticipate that progress will continue to accelerate leading to improved disease understanding, increased usage of 3d printing, and an increase in individualised care based on each patient's susceptibility.

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Conflict of Interest

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Paul Rodham: Writing – original draft. **Peter V Giannoudis:** Writing – review & editing.

Supplementary materials

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