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REVIEW ARTICLE

Multimodality imaging review of the post-amputation stump pain

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ABSTRACT

Limb amputation is one of the oldest known surgical procedures performed for a variety of indications. Little surgical technical improvements have been made since the first procedure, but perioperative and post-operative refinements have occurred over time. Post-amputation pain (PAP) of the stump is a common complication but is an extremely challenging condition to treat. Imaging allows early diagnosis of the underlying cause so that timely intervention is possible to minimize physical disability with its possible psychological and socioeconomic implications. A multidisciplinary approach should be taken involving the rehabilitation medicine team, surgeon, prosthetist, occupational therapist and social workers. Conventional radiographs demonstrate the osseous origin of PAP while high-resolution ultrasound is preferred to assess soft-tissue abnormalities. These are often the first-line investigations. MRI remains as a problem-solving tool when clinical and imaging findings are equivocal. This article aimed to raise a clear understanding of common pathologies expected in the assessment of PAP. A selection of multimodality images from our Specialist Mobility and Rehabilitation Unit are presented so that radiologists are aware of and recognize the spectrum of pathological conditions involving the amputation stump. These include but are not limited to aggressive bone spurs, heterotopic ossification, soft-tissue inflammation (stump bursitis), collection, nervosae, osteomyelitis etc. The role of the radiologist in reaching the diagnosis early is vital so that appropriate treatment can be instituted to limit long-term disability. The panel of authors hopes this article helps readers identify the spectrum of pathological conditions involving the post-amputation stump by recognizing the imaging features of the abnormalities in different imaging modalities.

INTRODUCTION

Limb amputation is one of the oldest known surgical procedures^{1,2} performed for a variety of clinical indications including peripheral vascular disease, trauma, tumour, infection, congenital anomalies etc. Amputation is carried out for diseased or injured limbs when attempts at salvage and reconstructions have been unsuccessful or are unrealistic emotionally or financially. There has been a steady increase in the number of all-cause amputations in the UK with total amputations of 16,010 carried out in the year 2013–14.³ The trend is likely to be linked with the increasing rate of diabetics with a record high rate of 135 diabetics undergoing amputation per week in the years 2011–14, as per the figures from Public Health England. Lower limb amputation accounts for the vast majority (90%) of the total amputees in the UK.⁴ Traumatic injury is the most common indication of upper limb amputation while peripheral vascular disease consistently remains a more frequent cause for lower limb amputations.⁴ Little

surgical technical improvements have been made since the first procedure, but perioperative and post-operative refinements have occurred over time.

Post-amputation pain (PAP) is a common complication with reported prevalence as high as 85%,^{5,6} but the concept was largely ignored by the medical establishment until recently. Among the traumatic amputees post-World War II, prevalence rates were consistently estimated at <5%.^{7,8} Moreover, the mechanism behind PAP during this time was falsely attributed to psychosocial phenomenon or ailment related to secondary gain.⁸ The challenge in managing PAP is widely recognized today owing to the plethora of aetiologies, which can be attributed as an underlying cause.

PAP can be isolated to the amputation stump or can occur as phantom pain, the latter being a more common cause with complex neurologic or psychosocial mechanisms

postulated as underlying mechanism.⁹ The radiological contribution in the diagnosis and management of phantom limb pain is very limited and is therefore beyond elaborative description of this clinical entity in this article. A clinician attending the patient with stump pain should be able to answer whether the stump pain is related to intrinsic or extrinsic causes, as outlined in Table 1. The conflict between prosthesis and residual limb is the cause of extrinsic stump pain and can be successfully treated by prosthetic socket modification. Intrinsic pain, on the other hand, is related to specific aetiologies warranting individualized treatment for successful pain relief.

Ironically, a variety of clinical entities responsible for PAP have identical non-specific clinical manifestations. Radiological assessment therefore has paramount clinical influence in identifying the underlying causes so that early treatment is instituted and rehabilitation of the amputees can be resumed. The morbidity associated with PAP is limited to not only the poor rehabilitation of the amputees but also its psychological and socioeconomic consequences. There have, however, been very limited data published in the literature evaluating PAP, most of which relate to neuroma. A comprehensive radiological review of stump pain has been published in the past,¹⁰ but the article focuses on conventional radiology and MRI. With technological advances in high-resolution ultrasound along with increasing availability of expertise in musculoskeletal ultrasound, the modality is becoming increasingly popular. In addition, ultrasound is radiation free, relatively cheap, portable and, more importantly, offers a platform for image-guided treatment of intrinsic causes of stump pain. Most centres these days use high-resolution ultrasound as a first-line radiological investigation in the assessment of PAP with application of MR as a problem-solving tool and treatment planning. There are a very limited

number of studies published in the literature regarding the utility of ultrasound in assessment of the post amputation pain. O'Reilly *et al*¹¹ reviewed 136 amputated sites in 133 patients who were symptomatic with high-resolution ultrasound and found stump neuroma to be the most common underlying cause followed by soft-tissue inflammation/oedema.

In this article, the utility of the various imaging modalities are discussed in relation to radiological appearances of common extrinsic and intrinsic causes of stump pain with a particular emphasis on high-resolution ultrasound as a first-line screening tool.

Stump neuroma

Stump neuromas occurring at the ends of the severed major nerves are a clinically significant cause of PAP. The damaged axon sprouts grow into surrounding scar tissues as a regenerative response to the nerve injury, forming neuromas.^{12,13} 3–5% of patient with injured peripheral nerve develop neuroma around the injured nerve as a complication of nerve injury.¹⁴ and many asymptomatic neuromas often remain undiagnosed. Two types of neuromas are encountered in clinical practice—terminal neuromas are usually the result of axonal proliferation of severed nerves at any direction without Schwann cell support and spindle neuroma away from the severed end as a result of repetitive microtrauma to the peripheral nerve by the localized scar tissue.¹⁰ The neuromas usually become apparent 1–12 months after amputation.¹⁵ Pain associated with neuroma formation is often difficult to distinguish from other causes, but clinical findings may reveal a soft-tissue mass. Pain relief following injection of local anaesthetic in the painful area is another clue to the diagnosis.

Imaging remains mainstay for the identification and localization of symptomatic neuromas. MRI remains the investigation of

Table 1. Intrinsic and extrinsic causes of post-amputation pain

Pathologies	Stipulated pathophysiology
Intrinsic causes	
Aggressive bone edges	Periosteal stripping during trauma or surgery of the bone to be retained
Heterotopic new bone formation	Traumatic muscular degeneration due to ischaemia or tissue expressions of BMP
Neuroma	Regenerative axonal proliferation of severed nerve or repetitive microtrauma of the peripheral nerve due to scar tissue
Osteomyelitis	Contiguous spread from local infection or haematogenous seeding of the micro-organism
Phantom pain	Idiopathic; complex neurologic and psychosocial mechanisms
Tumour recurrence	Microscopic metastases initially or tumour cells seeding intraoperatively
Extrinsic causes	
Stump bursitis	An adventitious bursae in response to the mechanical friction of soft tissue from the prosthetic socket
Bone bruises and stress reaction	Intensive unusual mechanical stress from body weight load at prosthesis–residual limb interface
Cutaneous lesions (abrasions, ulceration, folliculitis, eczema etc)	Confinement of stump in the prosthetic socket and resultant abnormal friction

BMP, bone morphogenic proteins.

choice for painful stump neuroma, which demonstrates a well-defined nodular mass of low signal intensity (SI) on T_1 weighted images and intermediate to high SI in T_2 weighted imaging (Figure 1c,d). Contrast enhancement is variable. With newer technical applications resulting in improved diagnostic accuracy of high-resolution ultrasound over the recent years, this has become the first-line investigation for assessment of the condition. In addition, ultrasound offers an image-guided platform to inject local anaesthetics for symptomatic relief to the patients. In the past, CT was mainstay investigation,¹⁶ which manifests as focal or generalized alteration in the calibre, size or contour of the nerve trunk in the affected stump (Figure 1a,b).

In a large number of patients, conservative measures are usually sufficient for treatment of the patients. These include physical therapy (ultrasound, massage, vibration etc.), medical intervention [local injection of corticosteroids and anaesthetics, non-steroidal anti-inflammatory drugs (NSAIDs) and tricyclic antidepressants] and cryotherapy.¹⁷ When these fail or in cases of complex neuromas, surgical intervention is necessary.¹⁸

Stump bursitis

The mechanical conflict between the amputation stump and prosthetic socket results in a range of inflammatory

conditions consisting of localized soft-tissue inflammation, adventitious bursa, bursitis and bone marrow oedema of the stump. Stump bursitis is a common complication of amputation stump with an incidence of 7.2%.¹⁹ Amputation stump bursitis, first described in 1903,²⁰ is adventitious bursa characterized histologically by mucoid and myxoid degeneration of the connective tissue. Clinical presentation varies from mechanical pain, inflammatory manifestations (erythema, swelling, local heat) and variation of stump volume to a fluctuating palpable mass.²¹

Plain radiography may reveal contributory osseous abnormalities at amputation site and/or soft-tissue thickening overlying the amputation end (Figure 2a). High-resolution ultrasound is often the first-line investigation in assessment of these patients. This reveals typical cobblestone appearances of the soft-tissue oedema or bursae distended with fluid (Figure 2b). The mainstay investigation of the condition remains MRI. Bursitis characteristically appears as low-SI areas on T_1 weighted images and bright SI on fluid-sensitive sequences and exhibits peripheral contrast enhancement on administration of gadolinium-based contrast agents. MRI offers more precise diagnosis and anatomic data that are readily useful for adaptation of prosthesis socket for individual amputee.¹⁹

Figure 1. Stump neuromas: high-resolution soft-tissue ultrasound (a) is showing two discrete hypoechoic lesions (arrows) typical of end neuromas. (b) An ultrasound image is showing a spindle neuroma (asterisk) away from the severed nerve end and characteristic "tail sign" of the involved nerve (arrow) proximally. Axial (c) and coronal (d) fat-suppressed MR images are showing the ovoid well-defined high-signal soft-tissue mass (arrows) characteristics of stump neuroma.

Critical cornerstone for bursitis management is prevention, so prosthetic socket modification to reduce mechanical friction over bursae has been proposed as first-line intervention. The clinical outcome is usually favourable with this intervention together with symptomatic treatment comprising rest, ice, compression stocking and elevation and NSAIDs.^{19,22}

Bone spurs/aggressive bone edges

Ectopic new bone formation at the edges of the amputation stump may lead to considerable pain in the residual limb and ill-fitting prostheses. Two mechanisms have been described²³—one way is the surgical excision of the periosteum over the bone to be retained and other is the widespread periosteal stripping by the primary trauma leading to amputation over the bone to be retained during amputation. In addition to PAP, bone spurs can cause overlying soft-tissue stress and ulceration, which can potentially be infected.²⁴

Conventional anteroposterior and lateral view radiograph can accurately assess bone spurs (Figure 3b), and high-resolution ultrasound is usually not the first-line investigation. However, initial assessment of PAP in our centre includes ultrasound; radiologists can expect to encounter this complication (Figure 3d) in patients at risk. Some authors even reported that ultrasound allows very early detection of the problem before it is apparent on plain radiograph.²⁵ MRI, with its inherent properties of higher contrast and soft-tissue resolution, remains a tool to delineate anatomical details of the bone spurs, depicts the associated soft-tissue inflammation and allows surgical planning for those resistant to conventional treatment.

Heterotopic ossification

Heterotopic ossification (HO) is a common and problematic clinical entity of post-traumatic ossification of the soft tissues that limits and/or delays the early rehabilitation of the amputees.^{26–28} Potter et al²⁶ reported 63% prevalence of all grades of HO in traumatic and combat-related amputees, of which 19% required surgical excision. Several studies in the literature have identified several risk factors for HO including high injury severity scores, amputations within the zone of blast injury, lower limb amputation and early wound complications at

the time of injury.^{26,28,29} Alfieri et al³⁰ have reported that an injury to the central nervous system is arguably the most important factor in both military and civilian trauma. HO has also been described in non-traumatic amputees.³¹

Patients with PAP usually present with firm swelling at the amputation site and/or abnormal popping noises while attempting a range of rehabilitative exercises. Loss of function is evident when it occurs around a joint and/or neurovascular structures and it can complicate the use of prosthesis. It is the most significant obstacle to functional mobility and return to active lifestyle.³⁰

Plain radiograph is highly specific for detection of established HO but lacks sensitivity in early non-mineralized HO, as calcium is deposited about 7–10 days after onset of symptoms. Initial patchy flocculent calcium coalesces as HO becomes mature over time (Figure 3a). Bone scintigraphy has traditionally been an investigation of choice for detection of early HO, as several studies have found marked vascular blush and increased blood pool precede the development of clinical HO by 2–4 weeks.^{32,33} Ultrasound has been found to be accurate in very early diagnosis of HO (Figure 3c), even within hours of clinical manifestation.²⁵ Ultrasound with its inherent advantages of safety, cost, reproducibility and portability is now the first-line investigation where expertise is available. It also allows early institution of the treatment for the patients.^{25,34} The role of CT and MRI scanning has not been well established in diagnosis but is found to be useful in delineating local anatomy prior to resection.³⁵

First-generation bisphosphonates have been used for the treatment and prevention of HO, but the efficacy of treatment is questionable and it has been shown to simply delay the mineralization.^{35,36} Both radiotherapy and NSAIDs have been demonstrated to be efficacious in the treatment of the condition.^{37–40} Once the function becomes limited, however, the only approach shown to be effective is surgical excision.³⁰ In most centres, however, surgical excision is limited to candidates in whom symptoms persist despite conservative management including rest, analgesics adjustment and socket modification in amputees. The rate of persistently symptomatic HO despite

Figure 2. Soft-tissue inflammation: conventional lateral radiograph of the stump (a) is demonstrating a bone spur (arrow) at the inferior edge of the stump. High-resolution soft-tissue ultrasound of the same patient (b) is revealing the bone spur (arrow) and associated bursal fluid distension (asterisk). An ultrasound image in a different patient (c) is showing a deep-seated collection (asterisk) and two sinus tracts (arrows) communicating the collection with skin surface.

Figure 3. Lateral conventional radiograph of an amputation stump (a) is showing heterotopic ossification (solid arrow) of the soft tissue, which in itself is swollen and is of higher density than the remainder of the soft tissues. These ossification foci are discontinuous from linear vascular calcification. High-resolution ultrasound (c) is confirming the presence of soft-tissue ossification focus (black arrow), with strong post-acoustic shadowing. Anteroposterior stump radiograph of another patient (b) is demonstrating a prominent bone spur within the lateral edge of the fibular stump (white arrow), which has been redemonstrated (curved arrow) on high-resolution ultrasound (d).

conservative management has been reported to be approximately 25% in amputees.²⁶

Post-operative wound infection/osteomyelitis

Amputation stump infection is a common post-operative complication with a potentially severe clinical outcome including reamputation, adding further morbidity or even death. The incidence of wound infection has been shown to range from 13 to 40%,^{41–44} although the majority of studies have been conducted in patients with critical peripheral vascular disease as an indication for amputation. Post-operative infection is adversely associated with revision surgery, time to heal, length of hospital stay or 30-day morbidity and mortality rates. Aggressive wound monitoring is therefore recommended in all patients.⁴⁵

The majority of the post-operative infection comprise of cellulitis characterized by swelling, pain and local erythema. High-resolution ultrasound reveals soft-tissue inflammatory changes with or without drainable soft-tissue collection. Power Doppler is a useful tool to detect multidirectional varying velocity flow within the inflamed tissue. Arranging an X-ray is usually good practice to exclude osteomyelitis, which would require aggressive

treatment to achieve successful treatment of local cellulitis.⁴⁶ In addition to the systemic antibiotics, the condition is successfully addressed with local wound care (debridement, dressing) and optimizing the host defence (diabetes control). On several instances, wound healing is delayed owing to deep-seated sinus or osteomyelitis.

A sinus is a blind-ended epithelium-lined tract that extends from the skin surface to the subcutaneous tissue. Often, there is a subcutaneous cavity (Figure 2c) in relation to the deep end of the sinus, which is a potential space for abscess formation. High-resolution ultrasound is the initial investigation tool to demonstrate the sinus tract communication between cutaneous surface and deeper soft tissue (Figure 2c). It also facilitates guided drainage of any soft-tissue collection.⁴⁷ A cavity may or may not be evident. Sinogram reveals the extent of the tract. MRI offers better anatomical depiction of the tract and can be used as a problem-solving tool, which positively impacts on the decision regarding choice of treatment. Surgical intervention is most effective in managing a sinus;⁴⁸ however, further surgery may not be appropriate management for amputees in view of the poor rehabilitation outcome. The decision regarding choice of

treatment should be carefully optimized holistically in multi-disciplinary team meetings.

Stump osteomyelitis can occur as an early or late complication of the procedure. It is a result of local spread from the neighbouring soft-tissue infection, haematogenous spread or late recurrence of clinically occult septic focus. In a 10-year retrospective study by Dutronc *et al*,⁴⁹ the presence of osteomyelitis required higher surgical revisions in addition to antibiotic therapy when compared with soft-tissue infection alone. Plain radiographic demonstration of bone destruction, osteosclerosis and periosteal reaction (Figure 4a) is neither sensitive nor specific for the detection of osteomyelitis in post-amputation stump; however, its utility for comparative studies is particularly important in raising suspicion of the complication and assessing the treatment response. Ultrasound may reveal bony irregularities on the background of soft-tissue inflammation (Figure 4b), but again this is non-specific in post-operative residual limb. Bone scintigraphy (Figures 5c,d) is sensitive for local inflammatory reaction but is non-specific. MR is more sensitive and is the imaging investigation of choice (Figures 4c,d and 5a,b) to demonstrate extent of bone involvement, adjacent soft-tissue changes and maps the possible local collection prior to drainage.⁵⁰ CT is particularly useful in demonstrating osseous anatomy and detecting small sequestra, which is occult to MRI.

Stress fractures and bone bruises

Post-amputation prosthetic rehabilitation alters the body biomechanics such that prosthesis-residual limb interface is forced

to tolerate the entire load of body weight. As the amputation stump is normally not subjected to such an intensive unusual mechanical stress, the residual limb responds by either remodelling itself to become load tolerant or developing an inflammatory reaction in the bone and/or soft tissue.⁵¹ Stress fractures and bone bruises in the residual limb are as a result of the inflammatory response to the uneven mechanical stress at the interface.

Conventional radiography is initially normal, contributing to the delayed diagnosis of the condition. Appearance of callus formation usually 2–3 weeks after the onset of symptoms confirms the diagnosis.⁵² Bone scintigraphy and MRI allow earlier diagnosis, with MRI (Figure 6) having added benefits of precise anatomic details so that it helps in correcting the shape of the socket.

Prosthetic socket modification designed to reduce the mechanical load at the pressure points of the residual limb is the treatment of choice.

Tumour recurrence

Local tumour recurrence may present as painful stump as an early or late complication of the procedure. Microscopic metastases at initial stage or intraoperative tumour seeding are the postulated mechanisms. Conventional radiography (Figure 7a,c) is the first-line investigation, but MRI (Figure 7b,d) is the imaging modality of choice.⁴⁹ Surgical resection of the recurrent tumour is necessary in patients who are suitable.

Figure 4. Osteomyelitis: conventional radiograph (a) is revealing osseous destruction and periosteal new bone formation (solid arrow) at the stump end. An ultrasound image of the same patient (b) is demonstrating bony irregularities with periosteal reaction (curved arrow) and adjacent soft-tissue inflammatory changes (star). Fat-suppressed sagittal T_2 weighted (T_2W) (c) and axial T_2W (d) MR images are confirming the presence of the intramedullary abscess.

Figure 5. Osteomyelitis: coronal T_1 weighted (a) and coronal short tau inversion-recovery (b) MR images are demonstrating extensive soft-tissue inflammation (arrows) and bone marrow oedema (curved arrow) compatible with stump soft-tissue infection with local contagious spread of soft-tissue infection resulting in stump osteomyelitis. A 4-h delayed planar bone scintigram image (c) of the same patient is confirming avid tracer uptake (solid arrow) at the site of osteomyelitis. The degenerative pattern of uptake within the ipsilateral knee can be noted. A Leukoscan image (d) is confirming avid uptake (thin arrow) in the same area.

CONCLUSION

A plethora of painful lesions can affect the amputation stump with non-specific associated clinical symptoms. Ultrasound is now being used as effective first-line investigation with increasing availability of expertise along with conventional radiography. In addition, ultrasound offers the advantage of being a useful tool for image-guided intervention in a number of amputees. Several other imaging modalities including bone scintigram and fluoroscopy have limited but

specific roles. MRI remains a problem-solving tool when physical examination and initial imaging do not detect the cause for a painful stump. Furthermore, MRI, with greater soft-tissue spatial and contrast resolution, is advantageous particularly in surgical planning of the patient. Overall, the article highlights the ever-increasing role of radiologists in detecting or treating patients with a painful stump, which may involve prosthetic modification, image-guided intervention, surgical revisions or an appropriate combination.

Figure 6. Stress reaction: axial T_1 weighted (a), axial short tau inversion-recovery (STIR) (b) and coronal STIR (c) MRI sequences are demonstrating subtle oedema-like changes at the stump-prosthesis interface (arrows) compatible with normal marrow response to altered biomechanics following amputation. The well-defined marrow changes with no associated soft-tissue inflammatory response can be noted.

Figure 7. Tumour recurrence: conventional anteroposterior radiograph (a) of a young patient showing aggressive lytic lesion in medial tibial metaphysis (solid arrow). Coronal T_1 weighted MRI (b) is confirming the low-signal mass (white star), which was proven to be tibial sarcoma on histology. 3 years after the amputation, the patient presented with stump pain. Conventional radiograph (c) is revealing osseous destruction at the stump end (arrow). Coronal short tau inversion-recovery MR image (d) is showing tumour recurrence with extensive aggressive osseous abnormalities (black star) and soft-tissue component of the lesion.

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