Residual Limb Pain Is Not a Diagnosis

A Proposed Algorithm to Classify Postamputation Pain

Collin Clarke, MD, David R. Lindsay, MD,†‡ Srinivas Pyati, MD,§ and Thomas Buchheit, MD§*

Background: Although postamputation pain (PAP) syndromes have been described since the 16th century, taxonomy of these conditions remains ill-defined. The term "Residual Limb Pain" fails to distinguish between distinct diagnostic entities such as neuroma, complex regional pain syndrome, and somatic pathology. Even phantom limb pain (PLP), although easily distinguished from residual limb pain (RLP), has not been consistently delineated from other PAP syndromes.

Methods: A systematic review of the literature was conducted to identify the degree of delineation of various post amputation pain states and what diagnostic criteria were utilized if any. Furthermore, papers that involved treatment modalities were reviewed to determine efficacy of treatment.

Results: Of the 151 papers reviewed, none further categorized RLP into more specific diagnostic criteria. Furthermore, the literature contains numerous case reports, case series, letters to the editors, and grossly underpowered studies demonstrating significant positive results, yet few high-quality randomized controlled trials.

Conclusions: Describing and defining the distinct clinical entities, intuitively, is a prerequisite to developing optimal treatments. The reported variation in the incidence of PAP phenomena may well represent inconsistency in assessment tools and diagnostic categories rather than variation in prevalence of these conditions. In this paper, we review the historical evolution of the current understanding of these syndromes and propose an algorithm for uniform classification.

Key Words: residual limb pain, stump pain, phantom limb pain, postamputation pain, pain taxonomy

(*Clin J Pain* 2013;00:000–000)

Although the postamputation syndromes of phantom limb pain (PLP) and residual limb pain (RLP) are not new to the human condition, formal discussions of these afflictions were not noted in the medical literature until the mid-16th century. At that time, the French military surgeon Ambroise Paré noted that months after amputation, soldiers continued to complain of pain in the missing limb. In addition to the original descriptions of PLP, he contributed detailed descriptions of RLP to early medical texts.[1]

RLP is a common problem among amputees and has multiple etiologies, both neuropathic and nociceptive.[2,3] Although diagnoses of neuroma, complex regional pain syndrome (CRPS), and somatic pathology exist in the postamputation pain (PAP) literature, to date, there has not been a concerted effort to delineate these conditions in a formal manner in the context of PAP.

The first published description of RLP subtypes was in 1864. Silas Weir Mitchell labeled one clinical entity as neuromata (neuroma) and another as causalgia, which we now know as complex regional pain syndrome, type II (CRPS II).[4] The literature continued to highlight the neurological origins of RLP in 1948, with Craig[5] discussing neuromas and causalgia (CRPS II) as being mediators of RLP. More recently, Wiffen et al[3] describe characteristics of RLP, and assert that specific pathology needs to be identified, focusing on ruling out somatic causes.

Identification of CRPS II, or sympathetically mediated PAP, as a significant cause of pain after amputation was common during the civil war.[6] However, in the 1940s it was reported that causalgia was rare, occurring only in amputations that were not performed with care.[7] Diagnostic criteria for CRPS II in the postamputation patient may be challenging with the use of currently accepted criteria because the missing limb results in absence of many of the physical findings. Nonetheless, autonomic, sudomotor, trophic, and sensory changes are often found in the residual limb. The patient may not meet criteria for CRPS, but a CRPS-like syndrome appears to exist. Isakov et al[8] demonstrated a case series of Below-Knee-Amputation patients that would meet the Budapest criteria for CRPS.

The neuroma phenomenon has been well addressed in the literature; in the early 1940s much attention was focused on PAP as soldiers were returning from World War II. Histologic examination of neuromas revealed branching masses of Schwann cells with proliferating axons embedded in scar tissue. Neuromas have naked nerve endings that are devoid of myelin and are more likely to repeatedly fire within the local anoxic environment of scar tissue.[9] Neuroma sensitization yields changes in the central nervous system that result in wind-up and central sensitization.[3] Over time, the appreciation of neuroma has grown and it remains frequently listed as a predominant cause of RLP.[10]

The cause of pain in the residual limb is not limited to neuropathic mechanisms.[2] In evaluating a patient with RLP, it is important to discriminate between neuropathic and somatic pain, as this has implications for treatment options.[11] Infection, failure of flap closure, bone spurs, vascular insufficiency, or soft tissue inflammation around the prosthesis are all common causes of somatic pain.[12] A significant number of amputees who use prostheses have symptoms arising from improper prosthetic fit or

Received for publication December 15, 2011; accepted May 28, 2012.
From the *Department of Anesthesia and Perioperative Medicine, University of Western Ontario, Victoria Hospital, London, ON, Canada; †Duke University Medical Center; ‡Durham VA Medical Center; and §Department of Anesthesiology, Durham VA Medical Center, Duke University, Durham, NC.
Partly supported by the Congressionally Directed Medical Research Programs (CDMRDP) and the Department of Defense (DM102142), United States. The authors declare no conflict of interest.
Reprints: Collin Clarke, MD, Department of Anesthesia and Perioperative Medicine, University of Western Ontario, Victoria Hospital D2-315, 800 Commissioners Rd. E, London, ON, Canada N6A 5W9 (e-mail: cclarke@uwo.ca).

alignment, lack of proper training, development of poor habits, or compensation for a secondary physical limitation. The historical literature definitively supports the notion that RLP represents manifestations of somatic pain CRPS II, sensitized neuromas, or potentially diffuse/mosaic neuralgic pains.

Of the PAP syndromes, phantom pain has been most frequently described and characterized over time. The classical description of a phantom limb is the persistent perception of sensation or pain originating from a body part after it has been removed by amputation or trauma. The majority of patients report phantom sensations immediately after their amputation. Although few patients lacking phantom limb sensations report PLP, the majority of patients with PLP also describe sensations.[13]

Mitchell[6] solidified the concept of PLP within the medical literature in his 1872 text *Injuries of Nerves and Their Consequences*. In 1954, the term "phantom limb" was granted its own heading in Index Medicus, making it a defined medical phenomenon.[14]

It is an unfortunate truth that many patients have PLP without receiving medical treatment as many physicians, until recently, regarded this condition as psychiatric disease that was "in the patient's head."[15] Fortunately, Melzack[16] solidified a central model of PLP with the publishing of his neuromatrix theory, postulating that PLP originates from alterations in the neurosynaptic architecture after amputation. Imaging studies have supported the neuromatrix theory as a cause of phantom pain, establishing a correlation between the severity of PLP and the degree of adjacent sensory invasion into the deafferented area.

There seems to be a wide range of reported prevalence of RLP and PLP. This variability likely results not only from the sensitivity of tests used, but also with potential changes in severity over time. The prevalence of RLP in observational studies has been reported between 21%[17] and 74%.[18] Observational studies of PLP have cited prevalence as low as 35%[19] and as high as 85%.[20] Sherman, who reported PLP prevalence at 85%, postulated that the wide variations reported in PLP may be because of the way in which patient populations were interviewed. Prevalence values remain inconsistent, suggesting that there is still considerable variation in assessment techniques.

There is a need for a standardized assessment tool as well as a classification system for the different pain subtypes that may occur in the residual limb. The lack of assessment and classification systems has led to ambiguity in our understanding of postamputation RLP.[21] Therapeutic algorithms are likely to be easier to follow once we better understand the conditions we are treating.

In this paper, we systematically review and highlight the lack of a uniform classification system for PAP which yields diagnostic limitations. Furthermore, we propose a direction for future classification and investigation.

METHODS

In conjunction with the United States Department of Defense grant on Veteran Integrated Pain Evaluation Research, an oversight committee was formed to address the diagnostic variability that was identified within the PAP clinics at the Durham Veteran's Administration Medical Center (DVAMC) (Durham, NC). The committee consisted of 4 pain practitioners involved in PAP treatment at DVAMC and/or Duke University Medical Center (Durham, NC) and the principle investigator of Veteran Integrated Pain Evaluation Research. A structured search of the literature to investigate previous clinical trials on PAP was conducted. A PubMed database query for "stump pain" or "residual limb pain" or "phantom limb pain" yielded 2710 results. Further limiting this to human clinical trials reported in English decreased this to 151 papers (June 14, 2011). These papers were each reviewed to identify patient categorization or sole descriptions of specific entities of PAP states. The following questions were then posed: (1) Was a subtype of PAP studied? (2) If so what subtypes were described? (3) If the subtypes were identified, was there a diagnostic criteria or algorithm?

RESULTS

The search results, as aforementioned, yielded 151 papers. Sixty-six of these papers contained no description of a PAP state, often containing references of phantom sensations only or were completely unrelated to pain states. A further 9 papers referred only to PAP and did not further delineate actual symptoms or diagnosis from this. Forty papers identified PLP as a patient population within the study, however, did not specifically identify any other PAP demographic. Eight papers specifically categorized patients with RLP phenomenon. Twenty papers differentiated PAP into either PLP or RLP, without further subtype differentiation—this was the furthest of global categorization seen. Eight papers identified neuroma as a cause of RLP but did not speak to the identification or differentiation of this phenomenon from other known entities (Table 1).

Furthermore, when assessing proposed treatments of PAP it became clear that the only delineation that is commonly evident is for that of PLP and RLP. Although ideally every case of PLP could be successfully treated the clinical reality is bleak, with $<10\%$ of PLP and RLP patients stating that they get benefit from their treatments.[174] The unfortunate state of affairs is that the literature contains numerous case reports, case series, letters to the editors, and grossly underpowered studies demonstrating significant positive results, yet few high-quality randomized controlled trials have been conducted.[175] There is also little differentiation in the literature with regard to the treatment of PLP versus RLP.

A PubMed database review for human clinical trials in treatment of PLP yields 72 papers. Fifteen of these papers contained no specific intervention or trial or were not related to PLP, but rather to phantom sensation or other neuropathic phenomena.[34,40,47,64,71,79,80,110,118,124,130,135,157,171,173] A further 16 papers detailed periamputation interventions for the prevention of PLP or the assessment of predictive factors for PL.[22,29,45,52,58,76,95,98,101,120,127,137,143,144,149,160] Seventeen papers contained PLP patients as subjects, but analysis of their outcome data did not distinguish between PLP and RLP.[35,36,42,43,50,56,61,62,84,87,113,123,125,147,164,166,169] The remaining 24 studies either specifically assess PLP reduction as an outcome or report changes in PLP as a component of the study.[25,32,38,41,53–55,65,68,85,90,91,93,94,97,99,104,138,148,152,158,162,168,172] Studies within this group contain small numbers and yield conflicting information.

There is some encouraging data regarding the use of the ketamine in the treatment of PLP when compared with placebo.[38,138] Likewise, dextromethorphan, another

TABLE 1. Degree of Classification of Post-amputation Pain States Within Human Clinical Trails

	Populations Identified					
References	**No PAP**	**PAP Only**	**PLP Only**	**PLP and RLP**	**RLP Only**	**Subtypes of RLP**
Borghi et al[22]				X		
Lindenhovius et al[23]	X					
Sivan et al[24]		X				
de Roos et al[25]		X				
Bosmans et al[26]		X				
Walsh et al[27]	X					
Ang et al[28]	X					
Behr et al[29]				X		
Smyrniotis et al[30]	X					
Balcin et al[31]						X (only neuroma)
Casale et al[32]			X			
Hall et al[33]	X					
Raichle et al[34]				X		
Wu et al[35]		X				
Gruber et al[36]				X		States neuroma as a cause of both
Kang et al[37]	X					
Eichenberger et al[38]			X			
Kalteis et al[39]	X					
Manias and Williams[40]	X					
Chan et al[41]			X			
Owen et al[42]			X			
Lazorthes et al[43]			X			
Nabhan et al[44]			X			
Wilson et al[45]				X		
Heidari et al[46]		X				
Bach and Clement[47]	X					
Lenti et al[48]	X					
Canadian Orthopaedic Trauma Society[49]	X					
Moseley[50]			X			Discusses CRPS, not in PAP
Pessaux et al[51]	X					
Nikolajsen et al[52]				X		
Kern et al[53]			X			
Yamamoto et al[54]			X			
Brodie et al[55]			X			
Blankertz et al[56]	X					
Lin et al[57]					X	
Schley et al[58]			X			
Ertem et al[59]	X					
Inan et al[60]	X					
Smith et al[61]				X		
Saitoh et al[62]	X					
Thome et al[63]	X					
Dhillon and Horch[64]	X					
Harden et al[65]			X			
Cuignet et al[66]	X					
Ephraim et al[67]				X		
Wilder-Smith et al[68]				X		
Schaefer et al[69]	X					
Suputtitada and Suwanwela[70]	X					
Hunter et al[71]				X		
Kane et al[72]	X					
Chiodo and Miller[73]						X (neuroma only)
Wong et al[74]	X					
MacKenzie et al[75]		X				
Hayes et al[76]				X		
Ben Gal et al[77]	X					
Barnett-Cowan and Peters[78]			X			
MacLachlan et al[79]			X			
Moseley[80]	X					CRPS (but not as PAP)
Kornblum et al[81]	X					
Paqueron et al[82]	X					
Beldi et al[83]	X					

(*Continued*)

TABLE 1. (*continued*)

	Populations Identified					
References	**No PAP**	**PAP Only**	**PLP Only**	**PLP and RLP**	**RLP Only**	**Subtypes of RLP**
Robinson et al[84]				X		
Wiech et al[85]			X			
Gimbel et al[86]	X					
Saitoh et al[87]			X			
Schwenkreis et al[88]			X			
Millisdotter et al[89]	X					
Maier et al[90]			X			
Ben Abraham et al[91]			X			
Goh et al[92]	X					
Bone et al[93]			X			
Ben Abraham et al[94]			X			
Techanivate et al[95]	X					
Gentili et al[96]	X					
Wu et al[97]				X		
Lambert et al[98]				X		
Flor et al[99]			X			
Maruno et al[100]	X					
Chu[101]	X					
Karl et al[102]			X			
da Paz et al[103]	X					
Huse et al[104]			X			
Grusser et al[105]				X		
Nikolajsen et al[106]				X		
Belcher and Pandya[107]						X (neuroma only)
Bakheit et al[108]	X					
Devers and Galer[109]						X (neuroma only)
Isaacson et al[110]	X					
Buchner et al[111]	X					
Angrilli and Koster[112]			X			
Carroll et al[113]			X			
Paya et al[114]	X					
Combes et al[115]	X					
Pucher et al[116]			X			
Muhlnickel et al[117]		X				
Ramazanov et al[118]	X					
Sirnes et al[119]	X					
Nikolajsen et al[120]					X	
Ramos-e-Silva et al[121]	X					
Montoya et al[122]			X			
Kumar et al[123]			X			Mentions CRPS but not PAP
Persson et al[124]	X					
Lenz et al[125]		X				
Kosasih and Silver-Thorn[126]					X	
Nikolajsen et al[127]				X		
Chow et al[128]	X					
Montoya et al[129]			X			
Dasgupta et al[130]					X	
Yuksel et al[131]						X (neuroma only)
Postema et al[132]					X	
Nikolajsen et al[133]					X	
Barkun et al[134]	X					
Merimsky et al[135]				X		
Ersland et al[136]	X					
Pinzur et al[137]		X				
Nikolajsen et al[138]				X		
Singh et al[139]	X					
Hill et al[140]			X			
Hunter et al[141]	X					
Gonzalez-Fajardo et al[142]	X					
Jahangiri et al[143]				X		
Elizaga et al[144]			X			
Arena et al[145]	X					
Dorman et al[146]	X					

(*Continued*)

TABLE 1. (*continued*)

	Populations Identified					
References	**No PAP**	**PAP Only**	**PLP Only**	**PLP and RLP**	**RLP Only**	**Subtypes of RLP**
Broggi et al[147]			X			CRPS mentioned but not PAP
Jaeger and Maier[148]			X			
Sicuteri et al[149]	X					
Jonson et al[150]	X					
Bossaert et al[151]	X					
Katz and Melzack[152]			X			
Sane et al[153]	X					
Schreiber et al[154]	X					
Panerai et al[155]			X			
Chaitman et al[156]	X					
Katz et al[157]	X					
Chabal et al[158]						X (neuroma only)
Topol et al[159]	X					
Finsen et al[160]				X		
Crist et al[161]	X					
Lundeberg[162]			X			
Corsini et al[163]	X					
Swerdlow[164]			X			
Steardo et al[165]	X					
Scadding et al[166]						X (neuroma only)
Mueller[167]					X	
Winnem and Amundsen[168]			X			
Langohr et al[169]						X (neuroma only)
Thorpe et al[170]					X	
Nathan[171]	X					
Melzack[172]			X			
Brenning[173]	X					
Totals	66	9	40	20	8	8

CRPS indicates complex regional pain syndrome; PAP, postamputation pain; PLP, phantom limb pain; RLP, residual limb pain.

NMDA antagonist, has demonstrated efficacy in small case series and randomized control trials.[91,94] All NMDA antagonists, however, have not shown equal efficacy, as memantine failed in randomized controlled trials to demonstrate significant pain reductions in the PLP population.[85,90]

Antiepileptic medications are frequently utilized by pain physicians for various pain syndromes thought to be of neurogenic origins. Of this class, gabapentin is the only member that has been studied in a randomized controlled trial specific for PLP. A randomized, double-blind, placebo-controlled, cross-over study with 19 patients demonstrated significant reductions in pain intensity with use of gabapentin relative to placebo.[93] Gabapentin has also been studied in the immediate postoperative period in an attempt to prevent or reduce the incidence of PLP. Unfortunately, a randomized trial did not demonstrate efficacy as compared with placebo.[52] Other trials involving gabapentin have shown equivocal results as compared with placebo.[61] The antiepileptic drug Topiramate has also shown some promise, although experience is limited to a small case series.[65]

Tricyclic antidepressants have long demonstrated efficacy in many neuropathic pain conditions. Amitriptyline was studied in a randomized control study for management of PLP and RLP. It was found to have similar benefits in pain reduction for both conditions with an average daily dose of 56 mg/d and a low side-effect profile.[68]

Opioids are often the mainstay of analgesia in both acute and chronic pain conditions. Several studies have demonstrated that opioids are effective at helping manage PLP and appear to have greater benefit than other drug classes.[68,97] Furthermore, it has been demonstrated that opioids have an effect on central pain mechanisms and may partly reverse some of the cortical shifting seen in patients with phantom pain. One investigator noted the correlation between analgesic response to morphine and reduction in cortical reorganization.[104] However, it remains unclear if the central changes noted in this study persist beyond the initial treatment period.

Studies investigating the use of the hormone calcitonin to treat PLP have been conducted. Although the studies are small, it appears that calcitonin may be beneficial if utilized at the early onset of PLP.[148] Studies conducted farther from the onset of PLP have failed to demonstrate any benefit from its use.[38]

The expanding role of surgical intervention is evident within the medical literature. Case series and reports demonstrate successful management of PLP with the use of deep brain stimulation at a variety of sites including the thalamic sensory relay nucleus and central sulcus.[54,87] Although not specifically captured in the aforementioned review, there exist case series and reports of successful management of PLP with the use of spinal cord stimulation.[176,177] We are careful to suggest that this option is to be considered only when other conservative management has failed.

In addition to medical and interventional management, psychological and rehabilitative strategies play a successful role in the management of PLP. Psychological

training using a variety of strategies, including management in processing emotional and somatosensory memories related to the amputation, have been demonstrated as effective in pain reduction.[25] Furthermore, sensory discrimination training has been shown to not only reduce PLP but also to significantly influence cortical reorganization. Some of the most promising work, which may give support to the neuromatrix theory, is the work done with mirror box therapy.[41,55]

Additional reports and studies have demonstrated varying efficacy with transcutaneous electrical nerve stimulation units applied to various locations; including the periauricular area, contralateral limb, and stump.[152,168,172] A double-blind, randomized, crossover trial in a total of 30 leg amputees demonstrated that an electromagnetically shielded stump stocking significantly reduced the incidence and intensity of PLP.[53] Although no specific etiology can explain these findings, they are interesting nonetheless.

Outside of the limited drug trials noted above, there is a paucity of evidence regarding effective pharmaceutical treatment strategies for PLP. Future trials should focus on therapies for patients who have ongoing PLP despite medical therapy with amitriptyline, ketamine, and opioid medications. In addition, methods to decrease the incidence and severity of phantom pain should be investigated for use at the time of elective amputation.

As a distinct entity, RLP has been underrepresented in the literature. Studies frequently combine PLP and RLP into 1 single category—PAP. However, the etiology and manifestation of these conditions are entirely separate. Existing studies often contain low patient numbers and infrequently speak to whether the cause of the RLP is somatic or neuropathic.

A PubMed database query for human clinical trials in the treatment of postamputation stump pain yields a total of 35 papers. Twelve of these papers do not address interventions related to postamputation RLP management.[41,53,57,71,92,99,104,125,126,138,157,165] A further 14 studies involve interventions for the prevention of RLP or positive predictors for the development of RLP.[45,46,52,75,76,98,107,120,127,131,143,170] Another 3 studies do not specifically delineate in the results the difference in outcomes between PLP and RLP.[35,61,160] This leaves 6 studies that note outcomes specific to RLP.

Wilder-Smith et al[68] demonstrated efficacy of both tramadol and amitriptyline in a 3-armed randomized control trial. Patients received individually titrated doses of tramadol, placebo (double-blind comparison), or amitriptyline (open comparison). Nonresponders were crossed over to the alternative active treatment. Eighty-one percent of patients who failed treatment in one arm saw success in another arm. This highlights the fact that RLP may have different etiologies and trialing a second medication may be very successful. In a randomized, double-blind, active-placebo-controlled, crossover trial with 32 patients, lidocaine and morphine were both found to be effective at ameliorating self-reported pain in the residual limb. Interestingly, in the same study only morphine was found to be effective on PLP.[97] Although there have been a few successful reports of NMDA antagonists for the management of PLP, the use of this drug class for RLP is sparse. This literature search provided a single case report of a single ketamine infusion giving pain relief for 31 hours to a patient with RLP.[133] An observational study of 20 RLP patients by Combes[178] showed efficacy of the dopamine antagonist tiapride in reduction of RLP, demonstrating an increased tolerance and duration of prosthesis use. These results, however, have not been reproduced elsewhere.

As neuroma is believed to be a significant mediator of RLP in many patients, it is logical that interventions performed on this trigger may have potential benefit. Although local anesthetic and steroid injections are frequently performed in the treatment of neuroma-related pain,[179] this treatment is not well supported with controlled trials. Neurolytic therapies using cryoablation and injection of phenol have also been used with success.[36,180] In a prospective manner, Gruber et al[36] demonstrated significant reductions in pain among 82 patients treated with ultrasound-guided neuroma injection with phenol. In addition to steroid injection and neurolytic therapies, immune system modulators such as the anti–tumor necrosis-α drug etanercept have been demonstrated promising analgesia when injected perineurally in patients with traumatic amputation.[181] It is interesting to note that the 6 PAP soldiers in this series reported significant improvements not only in their visual analogue pain score for RLP, but also in their PLP.

There have been additional complementary and alternative medicine reports of analgesia with the use of aroma and music therapy for RLP, particularly during dressing changes.[72] This review of the literature makes it apparent that there is no accepted documented system for differentiating PAP into specific categories; at best these patients are subclassified into RLP or PLP.

DISCUSSION

Identifying the need of a formal diagnostic algorithm for PAP a series of committee meetings were held over approximately 12 months conducted in think tank type sessions with several didactic presentations of solutions eventually culminating in a consensus among committee members, identifying 5 clinically distinct diagnoses. The result was the Durham Pain Investigations Group, Post-Amputation Pain Algorithm (DPIG-PAPA).

The DPIG-PAPA, utilizing simple questions, allows practitioners at almost any level of training, to classify

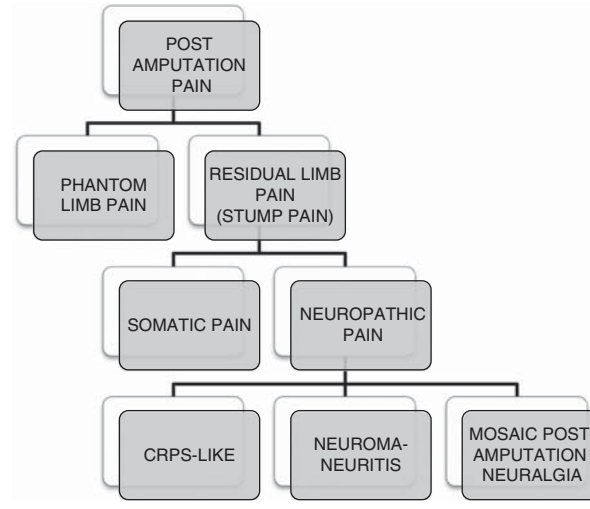

FIGURE 1. Proposed taxonomy of postamputation pain.

patients into one of the following categories: (1) PLP, (2) somatic RLP, (3) neuroma/neuritis RLP, (4) CRPS-like RLP, (5) mosaic postamputation neuralgia (MPAN) (Fig. 1). With the exception of MPAN these classifications are well embedded within the literature and lexicon of pain practice. MPAN is a classification developed in recognition that a small subset of patients present with a mixed neuropathic picture not easily delineated into typical diagnoses. The simple questions in conjunction with the validated Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale (sensitivity 81% to 91%, specificity 80% to 94%)[182] and the Budapest Clinical Criteria for Complex Regional Pain Syndrome (sensitivity 70%, specificity 94%)[183] have been readily used and are now well accepted within the DVAMC pain clinic. One weakness noted of this algorithm is that the LANSS criteria traditionally delineate outcomes into the likeliness or the unlikeliness of neuropathic pain. In order for the DPIG-PAPA to be a useful tool we felt it was important to assert patients into neuropathic or somatic pain pathologies. With the sensitivity and specificity of the LANSS criteria approaching that of other "gold standards," such as the Budapest criteria, we did not foresee any significant detriment to this. Certainly we have not experienced any issues with its application and use in our center.

PAP: Conclusions and Future Directions

Similar to the improvements in cancer therapy that evolve after receptor and biomarker classification of tumors, we foresee improvements in the treatment of amputation pain when the various subtypes are better recognized and treated as discreet clinical conditions. Although descriptions of postamputation sensation and pain syndromes have clearly been recorded in the recent and remote past, we still lack a uniform approach to PAP subtype classification.

Diagnostic clarity is of increasing importance given the recent global conflicts with both military and civilian casualties. Describing and defining the distinct clinical entities, especially in regards to RLP, is a likely prerequisite to developing optimal treatments. An intervention that may be effective for a sensitized neuroma may not be effective for more diffuse symptoms. Treatments for somatic and soft-tissue pathology may not alleviate the pain of nerve injury. Lumping widely disparate pathologic states together in clinical trials is likely to mask the effectiveness of these treatments for any individual PAP subtype. We propose a common classification system for the study of PAP that should allow for the development of disease-specific therapies and allow these to be evaluated in a more systematic way.

ACKNOWLEDGMENT

The authors thank Talia Schwartz, BS, Department of Anesthesia, Durham VA, Durham North Carolina, USA for her helpful comments in the preparation of this manuscript.

REFERENCES

1. Paré Ambroise. La Maniere De Traicter Les Playes Faictes Tant Par Hacquebutes, Que Par Fleches: & Les Accidentz D'icelles, Comme Fractures & Caries Des Os, Grangrene & Mortification; Avec Les Pourtraictz Des Instrumentz Necessaires Pour Leur Curation. Et La Methode De Curer Les Combustions Principalement Faictes Par La Pouldre a Canon ... Paris: Arnoul L'Angelie, 1552. Print.
2. Nikolajsen L, Ilkjaer S, Kroner K, et al. The influence of preamputation pain on postamputation stump and phantom pain. *Pain*. 1997;72:393–405.
3. Wiffen P, Meynadier J, Dubois M, et al. Diagnostic and treatment issues in postamputation pain after landmine injury. *Pain Med*. 2006;7(suppl 2):S209–S212.
4. Mitchell S. Weir, George R. Morehouse, and William W. Keen. Gunshot Wounds and Other Injuries of Nerves. Philadelphia: Lippincott, 1864. Print.
5. JD Craig. The phantom limb. *Postgrad Med J*. 1948;24: 643–648.
6. Mitchell Silas Weir. Injuries of Nerves and Their Consequences. London: n.p., 1872. Print.
7. Pretty HG. Role of the sympathetic nervous system in traumatic surgery as applied to fractures, causalgias and amputation stumps. *Am J Surg*. 1947;74:527–529.
8. Isakov E, Susak Z, Korzets A. Reflex sympathetic dystrophy of the stump in below-knee amputees. *Clin J Pain*. 1992;8:270–275.
9. White J. Pain after amputation and its treatment. *JAMA*. 1944;124:6.
10. Sehirlioglu A, Ozturk C, Yazicioglu K, et al. Painful neuroma requiring surgical excision after lower limb amputation caused by landmine explosions. *Int Orthop*. 2009;33: 533–536.
11. Nikolajsen L, Jensen TS. Phantom limb pain. *Br J Anaesth*. 2001;87:107–116.
12. McIntosh J, Earnshaw JJ. Antibiotic prophylaxis for the prevention of infection after major limb amputation. *Eur J Vasc Endovasc Surg*. 2009;37:696–703.
13. Kooijman CM, Dijkstra PU, Geertzen JH, et al. Phantom pain and phantom sensations in upper limb amputees: an epidemiological study. *Pain*. 2000;87:33–41.
14. Patterson R. Phantom limbs still a ghostly phenomenon. *CMAJ*. 1992;146:2036–2038.
15. Machin P, de C Williams AC. Stiff upper lip: coping strategies of World War II veterans with phantom limb pain. *Clin J Pain*. 1998;14:290–294.
16. Melzack R. Phantom limbs and the concept of a neuromatrix. *Trends Neurosci*. 1990;13:88–92.
17. Jensen TS, Krebs B, Nielsen J, et al. Immediate and long-term phantom limb pain in amputees: incidence, clinical characteristics and relationship to pre-amputation limb pain. *Pain*. 1985;21:267–278.
18. Smith DG, Ehde DM, Legro MW, et al. Phantom limb, residual limb, and back pain after lower extremity amputations. *Clin Orthop Relat Res*. 1999;361:29–38.
19. Melzack R. Phantom limb pain: implications for treatment of pathologic pain. *Anesthesiology*. 1971;35:409–419.
20. Sherman RA, Sherman CJ. Prevalence and characteristics of chronic phantom limb pain among American veterans. Results of a trial survey. *Am J Phys Med*. 1983;62:227–238.
21. Loeser J. The management of pain. In: Bonica J, ed. *The Management of Pain*. 2nd ed. Philadelphia: Lea & Febiger; 1990:913–918.
22. Borghi B, D'Addabbo M, White PF, et al. The use of prolonged peripheral neural blockade after lower extremity amputation: the effect on symptoms associated with phantom limb syndrome. *Anesth Analg*. 2010;111:1308–1315.
23. Lindenhovius AL, Doornberg JN, Ring D, et al. Health status after open elbow contracture release. *J Bone Joint Surg Am*. 2010;92:2187–2195.
24. Sivan M, Stoppard E, Kirker S. Alteration in phantom pain and sensation with visceral movement. *PM R*. 2010;2:576–578.
25. de Roos C, Veenstra AC, de Jongh A, et al. Treatment of chronic phantom limb pain using a trauma-focused psychological approach. *Pain Res Manag*. 2010;15:65–71.
26. Bosmans JC, Geertzen JH, Post WJ, et al. Factors associated with phantom limb pain: a 31/2-year prospective study. *Clin Rehabil*. 2010;24:444–453.
27. Walsh LD, Gandevia SC, Taylor JL. Illusory movements of a phantom hand grade with the duration and magnitude of motor commands. *J Physiol*. 2010;588(pt 8):1269–1280.

28. Ang DC, Chakr R, Mazzuca S, et al. Cognitive-behavioral therapy attenuates nociceptive responding in patients with fibromyalgia: a pilot study. *Arthritis Care Res*. 2010;62:618–623.
29. Behr J, Friedly J, Molton I, et al. Pain and pain-related interference in adults with lower-limb amputation: comparison of knee-disarticulation, transtibial, and transfemoral surgical sites. *J Rehabil Res Dev*. 2009;46:963–972.
30. Smyrniotis V, Arkadopoulos N, Kyriazi MA, et al. Does internal stenting of the pancreaticojejunostomy improve outcomes after pancreatoduodenectomy? A prospective study. *Langenbecks Arch Surg*. 2010;395:195–200.
31. Balcin H, Erba P, Wettstein R, et al. A comparative study of two methods of surgical treatment for painful neuroma. *J Bone Joint Surg Br*. 2009;91:803–808.
32. Casale R, Ceccherelli F, Labeeb AA, et al. Phantom limb pain relief by contralateral myofascial injection with local anaesthetic in a placebo-controlled study: preliminary results. *J Rehabil Med*. 2009;41:418–422.
33. Hall JA, Beuerlein MJ, McKee MD, Canadian Orthopaedic Trauma Society. Open reduction and internal fixation compared with circular fixator application for bicondylar tibial plateau fractures. Surgical technique. *J Bone Joint Surg Am*. 2009;91(suppl 2):pt 1):74–88.
34. Raichle KA, Hanley MA, Molton I, et al. Prosthesis use in persons with lower- and upper-limb amputation. *J Rehabil Res Dev*. 2008;45:961–972.
35. Wu CL, Agarwal S, Tella PK, et al. Morphine versus mexiletine for treatment of postamputation pain: a randomized, placebo-controlled, crossover trial. *Anesthesiology*. 2008;109:289–296.
36. Gruber H, Glodny B, Kopf H, et al. Practical experience with sonographically guided phenol instillation of stump neuroma: predictors of effects, success, and outcome. *Am J Roentgenol*. 2008;190:1263–1269.
37. Kang L, Akelman E, Weiss AP. Arthroscopic versus open dorsal ganglion excision: a prospective, randomized comparison of rates of recurrence and of residual pain. *J Hand Surg Am*. 2008;33:471–475.
38. Eichenberger U, Neff F, Sveticic G, et al. Chronic phantom limb pain: the effects of calcitonin, ketamine, and their combination on pain and sensory thresholds. *Anesth Analg*. 2008;106:1265–1273.
39. Kalteis M, Berger I, Messie-Werndl S, et al. High ligation combined with stripping and endovenous laser ablation of the great saphenous vein: early results of a randomized controlled study. *J Vasc Surg*. 2008;47:822–829; discussion 829.
40. Manias E, Williams A. Communication between patients with chronic kidney disease and nurses about managing pain in the acute hospital setting. *J Clin Nurs*. 2007;16(11C):358–367.
41. Chan BL, Witt R, Charrow AP, et al. Mirror therapy for phantom limb pain. *N Engl J Med*. 2007;357:2206–2207.
42. Owen SL, Green AL, Nandi DD, et al. Deep brain stimulation for neuropathic pain. *Acta Neurochir Suppl*. 2007;97(pt 2):111–116.
43. Lazorthes Y, Sol JC, Fowo S, et al. Motor cortex stimulation for neuropathic pain. *Acta Neurochir Suppl*. 2007;97(pt 2): 37–44.
44. Nabhan A, Pape D, Pitzen T, et al. Radiographic analysis of fusion progression following one-level cervical fusion with or without plate fixation. *Zentralbl Neurochir*. 2007;68: 133–138.
45. Wilson JA, Nimmo AF, Fleetwood-Walker SM, et al. A randomised double blind trial of the effect of pre-emptive epidural ketamine on persistent pain after lower limb amputation. *Pain*. 2008;135:108–118.
46. Heidari SM, Saghaei M, Hashemi SJ, et al. Effect of oral ketamine on the postoperative pain and analgesic requirement following orthopedic surgery. *Acta Anaesthesiol Taiwan*. 2006;44:211–215.
47. Bach GL, Clement DB. Efficacy of Farabloc as an analgesic in primary fibromyalgia. *Clin Rheumatol*. 2007;26:405–410.
48. Lenti M, Cieri E, De Rango P, et al. Endovascular treatment of long lesions of the superficial femoral artery: results from a multicenter registry of a spiral, covered polytetrafluoroethylene stent. *J Vasc Surg*. 2007;45:32–39.
49. Canadian Orthopaedic Trauma Society. Open reduction and internal fixation compared with circular fixator application for bicondylar tibial plateau fractures. Results of a multicenter, prospective, randomized clinical trial. *J Bone Joint Surg Am*. 2006;88:2613–2623.
50. Moseley GL. Graded motor imagery for pathologic pain: a randomized controlled trial. *Neurology*. 2006;67:2129–2134.
51. Pessaux P, Kianmanesh R, Regimbeau JM, et al. Frey procedure in the treatment of chronic pancreatitis: short-term results. *Pancreas*. 2006;33:354–358.
52. Nikolajsen L, Finnerup NB, Kramp S, et al. A randomized study of the effects of gabapentin on postamputation pain. *Anesthesiology*. 2006;105:1008–1015.
53. Kern U, Altkemper B, Kohl M. Management of phantom pain with a textile, electromagnetically-acting stump liner: a randomized, double-blind, crossover study. *J Pain Symptom Manage*. 2006;32:352–360.
54. Yamamoto T, Katayama Y, Obuchi T, et al. Thalamic sensory relay nucleus stimulation for the treatment of peripheral deafferentation pain. *Stereotact Funct Neurosurg*. 2006;84:180–183.
55. Brodie EE, Whyte A, Niven CA. Analgesia through the looking-glass? A randomized controlled trial investigating the effect of viewing a 'virtual' limb upon phantom limb pain, sensation and movement. *Eur J Pain*. 2007;11:428–436.
56. Blankertz B, Dornhege G, Krauledat M, et al. The Berlin brain-computer interface: EEG-based communication without subject training. *IEEE Trans Neural Syst Rehabil Eng*. 2006;14:147–152.
57. Lin EE, Horasek S, Agarwal S, et al. Local administration of norepinephrine in the stump evokes dose-dependent pain in amputees. *Clin J Pain*. 2006;22:482–486.
58. Schley M, Topfner S, Wiech K, et al. Continuous brachial plexus blockade in combination with the NMDA receptor antagonist memantine prevents phantom pain in acute traumatic upper limb amputees. *Eur J Pain*. 2007;11:299–308.
59. Ertem K, Kekilli KE, Yagmur C, et al. Somatotropic reorganization in the brain after extremity replantation, revascularization and amputations: investigated by SPECT analysis. *Ulus Travma Acil Cerrahi Derg*. 2006;12:121–128.
60. Inan M, El Rassi G, Riddle EC, et al. Residual deformities following successful initial bone union in congenital pseudarthrosis of the tibia. *J Pediatr Orthop*. 2006;26:393–399.
61. Smith DG, Ehde DM, Hanley MA, et al. Efficacy of gabapentin in treating chronic phantom limb and residual limb pain. *J Rehabil Res Dev*. 2005;42:645–654.
62. Saitoh Y, Hirano S, Kato A, et al. Motor cortex stimulation for deafferentation pain. *Neurosurg Focus*. 2001;11:E1.
63. Thome C, Leheta O, Krauss JK, et al. A prospective randomized comparison of rectangular titanium cage fusion and iliac crest autograft fusion in patients undergoing anterior cervical discectomy. *J Neurosurg Spine*. 2006;4:1–9.
64. Dhillon GS, Horch KW. Direct neural sensory feedback and control of a prosthetic arm. *IEEE Trans Neural Syst Rehabil Eng*. 2005;13:468–472.
65. Harden RN, Houle TT, Remble TA, et al. Topiramate for phantom limb pain: a time-series analysis. *Pain Med*. 2005;6:375–378.
66. Cuignet O, Mbuyamba J, Pirson J. The long-term analgesic efficacy of a single-shot fascia iliaca compartment block in burn patients undergoing skin-grafting procedures. *J Burn Care Rehabil*. 2005;26:409–415.
67. Ephraim PL, Wegener ST, MacKenzie EJ, et al. Phantom pain, residual limb pain, and back pain in amputees: results of a national survey. *Arch Phys Med Rehabil*. 2005;86: 1910–1919.
68. Wilder-Smith CH, Hill LT, Laurent S. Postamputation pain and sensory changes in treatment-naive patients:

characteristics and responses to treatment with tramadol, amitriptyline, and placebo. *Anesthesiology*. 2005;103:619–628.
69. Schaefer M, Noennig N, Heinze HJ, et al. Fooling your feelings: artificially induced referred sensations are linked to a modulation of the primary somatosensory cortex. *Neuroimage*. 2006;29:67–73.
70. Suputtitada A, Suwanwela NC. The lowest effective dose of botulinum A toxin in adult patients with upper limb spasticity. *Disabil Rehabil*. 2005;27:176–184.
71. Hunter JP, Katz J, Davis KD. Dissociation of phantom limb phenomena from stump tactile spatial acuity and sensory thresholds. *Brain*. 2005;128(pt 2):308–320.
72. Kane FM, Brodie EE, Coull A, et al. The analgesic effect of odour and music upon dressing change. *Br J Nurs*. 2004;13: S4–S12.
73. Chiodo CP, Miller SD. Surgical treatment of superficial peroneal neuroma. *Foot Ankle Int*. 2004;25:689–694.
74. Wong J, Boyd R, Keenan NW, et al. Gait patterns after fracture of the femoral shaft in children, managed by external fixation or early hip spica cast. *J Pediatr Orthop*. 2004;24: 463–471.
75. MacKenzie EJ, Bosse MJ, Castillo RC, et al. Functional outcomes following trauma-related lower-extremity amputation. *J Bone Joint Surg Am*. 2004;86-A:1636–1645.
76. Hayes C, Armstrong-Brown A, Burstal R. Perioperative intravenous ketamine infusion for the prevention of persistent post-amputation pain: a randomized, controlled trial. *Anaesth Intensive Care*. 2004;32:330–338.
77. Ben Gal Y, Sternik L, Shinfeld A, et al. Long-term arm morbidity after radial artery harvesting for coronary bypass operation. *Heart Surg Forum*. 2004;7:E211–E213.
78. Barnett-Cowan M, Peters M. Does handedness influence the strength of phantom limb illusions in the virtual reality box? *Brain Cogn*. 2004;55:275–276.
79. MacLachlan M, Desmond D, Horgan O. Psychological correlates of illusory body experiences. *J Rehabil Res Dev*. 2003;40:59–65.
80. Moseley GL. Graded motor imagery is effective for long-standing complex regional pain syndrome: a randomised controlled trial. *Pain*. 2004;108:192–198.
81. Kornblum MB, Fischgrund JS, Herkowitz HN, et al. Degenerative lumbar spondylolisthesis with spinal stenosis: a prospective long-term study comparing fusion and pseudarthrosis. *Spine*. 2004;29:726–733; discussion 733–734.
82. Paqueron X, Leguen M, Gentili ME, et al. Influence of sensory and proprioceptive impairment on the development of phantom limb syndrome during regional anesthesia. *Anesthesiology*. 2004;100:979–986.
83. Beldi G, Muggli K, Helbling C, et al. Laparoscopic appendectomy using endoloops: a prospective, randomized clinical trial. *Surg Endosc*. 2004;18:749–750.
84. Robinson LR, Czerniecki JM, Ehde DM, et al. Trial of amitriptyline for relief of pain in amputees: results of a randomized controlled study. *Arch Phys Med Rehabil*. 2004;85:1–6.
85. Wiech K, Kiefer RT, Topfner S, et al. A placebo-controlled randomized crossover trial of the *N*-methyl-D-aspartic acid receptor antagonist, memantine, in patients with chronic phantom limb pain. *Anesth Analg*. 2004;98:408–413.
86. Gimbel H, Zobbe V, Andersen BM, et al. Randomised controlled trial of total compared with subtotal hysterectomy with one-year follow up results. *BJOG*. 2003;110: 1088–1098.
87. Saitoh Y, Kato A, Ninomiya H, et al. Primary motor cortex stimulation within the central sulcus for treating deafferentation pain. *Acta Neurochir Suppl*. 2003;87:149–152.
88. Schwenkreis P, Maier C, Pleger B, et al. NMDA-mediated mechanisms in cortical excitability changes after limb amputation. *Acta Neurol Scand*. 2003;108:179–184.
89. Millisdotter M, Stromqvist B, Jonsson B. Proximal neuromuscular impairment in lumbar disc herniation: a prospective controlled study. *Spine*. 2003;28:1281–1289.
90. Maier C, Dertwinkel R, Mansourian N, et al. Efficacy of the NMDA-receptor antagonist memantine in patients with chronic phantom limb pain—results of a randomized double-blinded, placebo-controlled trial. *Pain*. 2003;103:277–283.
91. Ben Abraham R, Marouani N, Weinbroum AA. Dextromethorphan mitigates phantom pain in cancer amputees. *Ann Surg Oncol*. 2003;10:268–274.
92. Goh JC, Lee PV, Chong SY. Stump/socket pressure profiles of the pressure cast prosthetic socket. *Clin Biomech*. 2003;18: 237–243.
93. Bone M, Critchley P, Buggy DJ. Gabapentin in postamputation phantom limb pain: a randomized, double-blind, placebo-controlled, cross-over study. *Reg Anesth Pain Med*. 2002;27:481–486.
94. Ben Abraham R, Marouani N, Kollender Y, et al. Dextromethorphan for phantom pain attenuation in cancer amputees: a double-blind crossover trial involving three patients. *Clin J Pain*. 2002;18:282–285.
95. Techanivate A, Ultchaswadi P, Chaedamphai E. Prevention of phantom sensations after spinal anesthesia. *J Med Assoc Thai*. 2002;85:207–214.
96. Gentili ME, Verton C, Kinirons B, et al. Clinical perception of phantom limb sensation in patients with brachial plexus block. *Eur J Anaesthesiol*. 2002;19:105–108.
97. Wu CL, Tella P, Staats PS, et al. Analgesic effects of intravenous lidocaine and morphine on postamputation pain: a randomized double-blind, active placebo-controlled, crossover trial. *Anesthesiology*. 2002;96:841–848.
98. Lambert A, Dashfield A, Cosgrove C, et al. Randomized prospective study comparing preoperative epidural and intraoperative perineural analgesia for the prevention of postoperative stump and phantom limb pain following major amputation. *Reg Anesth Pain Med*. 2001;26:316–321.
99. Flor H, Denke C, Schaefer M, et al. Effect of sensory discrimination training on cortical reorganisation and phantom limb pain. *Lancet*. 2001;357:1763–1764.
100. Maruno N, Kaminaga T, Mikami M, et al. Activation of supplementary motor area during imaginary movement of phantom toes. *Neurorehabil Neural Repair*. 2000;14:345–349.
101. Chu NS. Phantom finger phenomena and the effects of toe-to-finger transplantation. *Neurorehabil Neural Repair*. 2000;14:277–285.
102. Karl A, Birbaumer N, Lutzenberger W, et al. Reorganization of motor and somatosensory cortex in upper extremity amputees with phantom limb pain. *J Neurosci*. 2001;21: 3609–3618.
103. da Paz AC Jr, Braga LW, Downs JH III. A preliminary functional brain study on amputees. *Appl Neuropsychol*. 2000;7:121–125.
104. Huse E, Larbig W, Flor H, et al. The effect of opioids on phantom limb pain and cortical reorganization. *Pain*. 2001;90:47–55.
105. Grusser SM, Winter C, Muhlnickel W, et al. The relationship of perceptual phenomena and cortical reorganization in upper extremity amputees. *Neuroscience*. 2001;102:263–272.
106. Nikolajsen L, Ilkjaer S, Jensen TS. Relationship between mechanical sensitivity and postamputation pain: a prospective study. *Eur J Pain*. 2000;4:327–334.
107. Belcher HJ, Pandya AN. Centro-central union for the prevention of neuroma formation after finger amputation. *J Hand Surg Br*. 2000;25:154–159.
108. Bakheit AM, Thilmann AF, Ward AB, et al. A randomized, double-blind, placebo-controlled, dose-ranging study to compare the efficacy and safety of three doses of botulinum toxin type A (Dysport) with placebo in upper limb spasticity after stroke. *Stroke*. 2000;31:2402–2406.
109. Devers A, Galer BS. Topical lidocaine patch relieves a variety of neuropathic pain conditions: an open-label study. *Clin J Pain*. 2000;16:205–208.
110. Isaacson SA, Funderburk M, Yang J. Regulation of proprioceptive memory by subarachnoid regional anesthesia. *Anesthesiology*. 2000;93:55–61.

111. Buchner H, Richrath P, Grunholz J, et al. Differential effects of pain and spatial attention on digit representation in the human primary somatosensory cortex. *Neuroreport*. 2000;11:1289–1293.
112. Angrilli A, Koster U. Psychophysiological stress responses in amputees with and without phantom limb pain. *Physiol Behav*. 2000;68:699–706.
113. Carroll D, Joint C, Maartens N, et al. Motor cortex stimulation for chronic neuropathic pain: a preliminary study of 10 cases. *Pain*. 2000;84:431–437.
114. Paya K, Rauhofer U, Rebhandl W, et al. Perforating appendicitis. An indication for laparoscopy? *Surg Endosc*. 2000;14:182–184.
115. Combes X, Cerf C, Bouleau D, et al. The effects of residual pain on oxygenation and breathing pattern during morphine analgesia. *Anesth Analg*. 2000;90:156–160.
116. Pucher I, Kickinger W, Frischenschlager O. Coping with amputation and phantom limb pain. *J Psychosom Res*. 1999;46:379–383.
117. Muhlnickel W, Lutzenberger W, Flor H. Localization of somatosensory evoked potentials in primary somatosensory cortex: a comparison between PCA and MUSIC. *Brain Topogr*. 1999;11:185–191.
118. Ramazanov R, Dreval ON, Akatov OV, et al. Ultrasound microneurosurgery. *Neurol Res*. 1999;21:73–76.
119. Sirnes PA, Molstad P, Myreng Y, et al. Predictors for restenosis after angioplasty of chronic coronary occlusions. *Int J Cardiol*. 1998;67:111–118.
120. Nikolajsen L, Ilkjaer S, Jensen TS. Effect of preoperative extradural bupivacaine and morphine on stump sensation in lower limb amputees. *Br J Anaesth*. 1998;81:348–354.
121. Ramos-e-Silva M, Marques SA, Gontijo B, et al. Efficacy and safety of itraconazole pulse therapy: Brazilian multicentric study on toenail onychomycosis caused by dermatophytes. *J Eur Acad Dermatol Venereol*. 1998;11:109–116.
122. Montoya P, Ritter K, Huse E, et al. The cortical somatotopic map and phantom phenomena in subjects with congenital limb atrophy and traumatic amputees with phantom limb pain. *Eur J Neurosci*. 1998;10:1095–1102.
123. Kumar K, Toth C, Nath RK, et al. Epidural spinal cord stimulation for treatment of chronic pain—some predictors of success. A 15-year experience. *Surg Neurol*. 1998;50:110–120; discussion 120–121.
124. Persson J, Hasselstrom J, Wiklund B, et al. The analgesic effect of racemic ketamine in patients with chronic ischemic pain due to lower extremity arteriosclerosis obliterans. *Acta Anaesthesiol Scand*. 1998;42:750–758.
125. Lenz FA, Garonzik IM, Zirh TA, et al. Neuronal activity in the region of the thalamic principal sensory nucleus (ventralis caudalis) in patients with pain following amputations. *Neuroscience*. 1998;86:1065–1081.
126. Kosasih JB, Silver-Thorn MB. Sensory changes in adults with unilateral transtibial amputation. *J Rehabil Res Dev*. 1998;35: 85–90.
127. Nikolajsen L, Ilkjaer S, Christensen JH, et al. Randomised trial of epidural bupivacaine and morphine in prevention of stump and phantom pain in lower-limb amputation. *Lancet*. 1997;350:1353–1357.
128. Chow S, Bosco JJ, Heiss FW, et al. Successful treatment of post-cholecystectomy bile leaks using nasobiliary tube drainage and sphincterotomy. *Am J Gastroenterol*. 1997;92:1839–1843.
129. Montoya P, Larbig W, Grulke N, et al. The relationship of phantom limb pain to other phantom limb phenomena in upper extremity amputees. *Pain*. 1997;72:87–93.
130. Dasgupta AK, McCluskie PJ, Patel VS, et al. The performance of the ICEROSS prostheses amongst transtibial amputees with a special reference to the workplace—a preliminary study. Icelandic Roll on Silicone Socket. *Occup Med*. 1997; 47:228–236.
131. Yuksel F, Kislaoglu E, Durak N, et al. Prevention of painful neuromas by epineural ligatures, flaps and grafts. *Br J Plast Surg*. 1997;50:182–185.
132. Postema K, Hermens HJ, de Vries J, et al. Energy storage and release of prosthetic feet. Part 2: subjective ratings of 2 energy storing and 2 conventional feet, user choice of foot and deciding factor. *Prosthet Orthot Int*. 1997;21:28–34.
133. Nikolajsen L, Hansen PO, Jensen TS. Oral ketamine therapy in the treatment of postamputation stump pain. *Acta Anaesthesiol Scand*. 1997;41:427–429.
134. Barkun AN, Rezieg M, Mehta SN, et al. Postcholecystectomy biliary leaks in the laparoscopic era: risk factors, presentation, and management. McGill Gallstone Treatment Group. *Gastrointest Endosc*. 1997;45:277–282.
135. Merimsky O, Kollender Y, Inbar M, et al. Palliative major amputation and quality of life in cancer patients. *Acta Oncol*. 1997;36:151–157.
136. Ersland L, Rosen G, Lundervold A, et al. Phantom limb imaginary fingertapping causes primary motor cortex activation: an fMRI study. *Neuroreport*. 1996;8:207–210.
137. Pinzur MS, Garla PG, Pluth T, et al. Continuous postoperative infusion of a regional anesthetic after an amputation of the lower extremity. A randomized clinical trial. *J Bone Joint Surg Am*. 1996;78:1501–1505.
138. Nikolajsen L, Hansen CL, Nielsen J, et al. The effect of ketamine on phantom pain: a central neuropathic disorder maintained by peripheral input. *Pain*. 1996;67:69–77.
139. Singh V, Kumar P, Rai HS, et al. Postcholecystectomy problems and the role of endoscopic retrograde cholangiopancreatography. *Br J Clin Pract*. 1996;50:183–186.
140. Hill A, Niven CA, Knussen C. The role of coping in adjustment to phantom limb pain. *Pain*. 1995;62:79–86.
141. Hunter D, Smith Cole E, Murray JM, et al. Energy expenditure of below-knee amputees during harness-supported treadmill ambulation. *J Orthop Sports Phys Ther*. 1995;21: 268–276.
142. Gonzalez-Fajardo JA, Perez-Burkhardt JL, Mateo AM. Intraoperative fibrinolytic therapy for salvage of limbs with acute arterial ischemia: an adjunct to thromboembolectomy. *Ann Vasc Surg*. 1995;9:179–186.
143. Jahangiri M, Jayatunga AP, Bradley JW, et al. Prevention of phantom pain after major lower limb amputation by epidural infusion of diamorphine, clonidine and bupivacaine. *Ann R Coll Surg Engl*. 1994;76:324–326.
144. Elizaga AM, Smith DG, Sharar SR, et al. Continuous regional analgesia by intraneural block: effect on postoperative opioid requirements and phantom limb pain following amputation. *J Rehabil Res Dev*. 1994;31:179–187.
145. Arena JG, Bruno GM, Brucks AG, et al. Reliability of an ambulatory electromyographic activity device for musculoskeletal pain disorders. *Int J Psychophysiol*. 1994;17:153–157.
146. Dorman BH, Conroy JM, Duc TA Jr, et al. Postoperative analgesia after major shoulder surgery with interscalene brachial plexus blockade: etidocaine versus bupivacaine. *South Med J*. 1994;87:502–505.
147. Broggi G, Servello D, Dones I, et al. Italian multicentric study on pain treatment with epidural spinal cord stimulation. *Stereotact Funct Neurosurg*. 1994;62:273–278.
148. Jaeger H, Maier C. Calcitonin in phantom limb pain: a double-blind study. *Pain*. 1992;48:21–27.
149. Sicuteri F, Nicolodi M, Fusco BM, et al. Idiopathic headache as a possible risk factor for phantom tooth pain. *Headache*. 1991;31:577–581.
150. Jonson G, Nilsson DM, Nilsson T. Cystic duct remnants and biliary symptoms after cholecystectomy. A randomised comparison of two operative techniques. *Eur J Surg*. 1991;157: 583–586.
151. Bossaert L, Conraads V, Pintens H. ST-segment analysis: a useful marker for reperfusion after thrombolysis with APSAC? The Belgian EMS Study Group. *Eur Heart J*. 1991;12:357–362.
152. Katz J, Melzack R. Auricular transcutaneous electrical nerve stimulation (TENS) reduces phantom limb pain. *J Pain Symptom Manage*. 1991;6:73–83.

153. Sane DC, Stump DC, Topol EJ, et al. Racial differences in responses to thrombolytic therapy with recombinant tissue-type plasminogen activator. Increased fibrin(ogen)olysis in blacks. The Thrombolysis and Angioplasty in Myocardial Infarction Study Group. *Circulation*. 1991;83:170–175.
154. Schreiber TL, Macina G, Bunnell P, et al. Unstable angina or non-Q wave infarction despite long-term aspirin: response to thrombolytic therapy with implications on mechanisms. *Am Heart J*. 1990;120:248–255.
155. Panerai AE, Monza G, Movilia P, et al. A randomized, within-patient, cross-over, placebo-controlled trial on the efficacy and tolerability of the tricyclic antidepressants chlorimipramine and nortriptyline in central pain. *Acta Neurol Scand*. 1990;82:34–38.
156. Chaitman BR, Thompson B, Wittry MD, et al. The use of tissue-type plasminogen activator for acute myocardial infarction in the elderly: results from thrombolysis in myocardial infarction phase I, open label studies and the thrombolysis in myocardial infarction phase II pilot study. The TIMI Investigators. *J Am Coll Cardiol*. 1989;14:1159–1165.
157. Katz J, France C, Melzack R. An association between phantom limb sensations and stump skin conductance during transcutaneous electrical nerve stimulation (TENS) applied to the contralateral leg: a case study. *Pain*. 1989;36:367–377.
158. Chabal C, Jacobson L, Russell LC, et al. Pain responses to perineuromal injection of normal saline, gallamine, and lidocaine in humans. *Pain*. 1989;36:321–325.
159. Topol EJ, George BS, Kereiakes DJ, et al. Comparison of two dose regimens of intravenous tissue plasminogen activator for acute myocardial infarction. *Am J Cardiol*. 1988;61:723–728.
160. Finsen V, Persen L, Lovlien M, et al. Transcutaneous electrical nerve stimulation after major amputation. *J Bone Joint Surg Br*. 1988;70:109–112.
161. Crist WM, Raney RB, Tefft M, et al. Soft tissue sarcomas arising in the retroperitoneal space in children. A report from the Intergroup Rhabdomyosarcoma Study (IRS) Committee. *Cancer*. 1985;56:2125–2132.
162. Lundeberg T. Relief of pain from a phantom limb by peripheral stimulation. *J Neurol*. 1985;232:79–82.
163. Corsini G, Bresci G, Capria A, et al. Sucralfate and carbenoxolone in the treatment of functional disturbances following partial gastrectomy. *Int J Tissue React*. 1984;6:185–188.
164. Swerdlow M. Anticonvulsant drugs and chronic pain. *Clin Neuropharmacol*. 1984;7:51–82.
165. Steardo L, Leo A, Marano E. Efficacy of baclofen in trigeminal neuralgia and some other painful conditions. A clinical trial. *Eur Neurol*. 1984;23:51–55.
166. Scadding JW, Wall PD, Parry CB, et al. Clinical trial of propranolol in post-traumatic neuralgia. *Pain*. 1982;14:283–292.
167. Mueller MJ. Comparison of removable rigid dressings and elastic bandages in preprosthetic management of patients with below-knee amputations. *Phys Ther*. 1982;62:1438–1441.
168. Winnem MF, Amundsen T. Treatment of phantom limb pain with TENS. *Pain*. 1982;12:299–300.
169. Langohr HD, Stohr M, Petruch F. An open and double-blind cross-over study on the efficacy of clomipramine (Anafranil) in patients with painful mono- and polyneuropathies. *Eur Neurol*. 1982;21:309–317.
170. Thorpe W, Gerber LH, Lampert M, et al. A prospective study of the rehabilitation of the above-knee amputee with rigid dressing. Comparison of immediate and delayed ambulation and the role of physical therapists and prosthetists. *Clin Orthop Relat Res*. 1979;143:133–137.
171. Nathan PW. Chlorprothixene (taractan) in post-herpetic neuralgia and other severe chronic pains. *Pain*. 1978;5:367–371.
172. Melzack R. Prolonged relief of pain by brief, intense transcutaneous somatic stimulation. *Pain*. 1975;1:357–373.
173. Brenning R. Motor manifestations in molimina crurum nocturna (including "restless legs"). *J Am Geriatr Soc*. 1971;19:700–708.
174. Sherman RA, Sherman CJ, Parker L. Chronic phantom and stump pain among American veterans: results of a survey. *Pain*. 1984;18:83–95.
175. Halbert J, Crotty M, Cameron ID. Evidence for the optimal management of acute and chronic phantom pain: a systematic review. *Clin J Pain*. 2002;18:84–92.
176. Viswanathan A, Phan PC, Burton AW. Use of spinal cord stimulation in the treatment of phantom limb pain: case series and review of the literature. *Pain Pract*. 2010;10:479–484.
177. Nielson KD, Adams JE, Hosobuchi Y. Phantom limb pain. Treatment with dorsal column stimulation. *J Neurosurg*. 1975;42:301–307.
178. Combes F. Amputation stump pain: a therapeutic study (author's transl). *Sem Hop*. 1980;56:245–247.
179. Fischler AH, Gross JB. Ultrasound-guided sciatic neuroma block for treatment of intractable stump pain. *J Clin Anesth*. 2007;19:626–628.
180. Neumann V, O'Connor RJ, Bush D. Cryoprobe treatment: an alternative to phenol injections for painful neuromas after amputation. *Am J Roentgenol*. 2008;191:W313; author reply W314.
181. Dahl E, Cohen SP. Perineural injection of etanercept as a treatment for postamputation pain. *Clin J Pain*. 2008;24:172–175.
182. Bennett M. The LANSS pain scale: the Leeds assessment of neuropathic symptoms and signs. *Pain*. 2001;92:147–157.
183. Harden RN, Bruehl S, Perez RS, et al. Validation of proposed diagnostic criteria (the "Budapest Criteria") for Complex Regional Pain Syndrome. *Pain*. 2010;150:268–274.

APPENDIX A: MASTER ALGORITHM

Step #1		
Does the patient percieve pain in part of the missing lim?	**YES**	**NO**
If **YES** then: ***Phantom Limb Pain***		
If **NO** then: Proceed to Step 2		
Step #2		
Complete **LANSS** screening tool to identify neuropathic pain (attached):		
If LANSS < 12 then: ***Somatic Pain***		
If LANNS ≥ 12 then: Proceed to Step 3		
Step #3		
Part A: Is the pain localized to a specific nerve distribution?:	**YES**	**NO**
Part B: Is there a Tinel's Sign?:	**YES**	**NO**
Part C: Complete the budapest criteria (attached), does the patient meet the budapest criteria?:	**YES**	**NO**
If Yes to A and or B but not C then: ***Neuroma/Neuritis***		
If Yes to A and/or B and C then: ***Mosaic Post-Amputation Neuralgia***		
If yes to only C then: ***CRPS-like***		

APPENDIX B: LANSS PAGE 1

The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale

Name..... Date

This pain scale can help to determine whether the nerves that are carrying your pain signals are working normally or not. It is important to find this out in case different treatments are needed to control your pain.

A. PAIN QUESTIONNAIRE

- Think about how your pain has felt over the last week.
- Please say whether any of the descriptions match your pain exactly.

1. Does your pain feel like strange, unpleasant sensations in your skin?
Words like pricking, tingling, pins and needles might describe these sensations.
a) NO – My pain doesn't really feel like this (0)
b) YES – I get these sensations quite a lot (5)

2. Does your pain make the skin in the painful area look different from normal?
Words like mottled or looking more red or pink might describe the appearance.
a) NO – My pain doesn't affect the colour of my skin (0)
b) YES – I've noticed that the pain does make my skin look different from normal (5)

3. Does your pain make the affected skin abnormally sensitive to touch?
Getting unpleasant sensations when lightly stroking the skin, or getting pain when wearing tight clothes might describe the abnormal sensitivity.
a) NO – My pain doesn't make my skin abnormally sensitive in that area (0)
b) YES – My skin seems abnormally sensitive to touch in that area (3)

4. Does your pain come on suddenly and in bursts for no apparent reason when you're still?
Words like electric shocks, jumping and bursting describe these sensations.
a) NO – My pain doesn't really feel like this (0)
b) YES – I get these sensations quite a lot (2)

5. Does your pain feel as if the skin temperature in the painful area has changed abnormally?
Words like hot and burning describe these sensations.
a) NO – I don't really get these sensations (0)
b) YES – I get these sensations quite a lot (1)

APPENDIX C: LANSS PAGE 2

Leeds Assessment of Neuropathic Symptoms and Signs (continued)
B. SENSORY TESTING
Skin sensitivity can be examined by comparing the painful area with a contralateral or adjacent non-painful area for the presence of allodynia and an altered pin-prick threshold (PPT).

1. Allodynia
Examine the response to lightly stroking cotton wool across the non-painful area and then the painful area. If normal sensations are experienced in the non-painful site, but pain or unpleasant sensations (tingling, nausea) are experienced in the painful area when stroking, allodynia is present.
a) NO – Normal sensations in both area (0)
b) YES – Allodynia in painful area only (5)

2. Altered pin-prick threshold
Determine the pin-prick threshold by comparing the response to a 23-gauge (blue) needle mounted inside a 2ml syringe barrel placed gently onto the skin in a non-painful and then painful areas.
If a sharp pin prick is felt in the non-painful area, but a different sensation is experienced in the painful area, eg. none/ blunt only (raised PPT) or a very painful sensation (lowered PPT), an altered PPT is present.
If a pinprick is not felt in either area, mount the syringe onto the needle to increase the weight and repeat.
a) NO – Equal sensation in both areas (0)
b) YES – Altered PPT in painful area (3)

SCORING:
Add values in parentheses for sensory description and examination findings to obtain overall score.

TOTAL SCORE (maximum 24) ***If score < 12, neuropathic mechanisms are unlikely to be contributing to the patient's pain. If score ≥ 12, neuropathic mechanisms are likely to be contributing to the patient's pain.***

APPENDIX D: MODIFIED BUDAPEST CRITERIA OF CRPS

Must report at least one symptom in three of the four categories:

Sensory: reports of hyperesthesia and/or allodynia	
Vasomotor: reports of temperature asymmetry and/or skin color changes and/or asymetry	
Sudomotor/edema: reports of edema and/or sweating changes and/or asymmetry	
Motor/Trophic: reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (nails, hair, skin)	
SCORE	

Must report at least one sign in 2 of the four categories:

Sensory: evidence of hyperesthesia(to pinprick) and/or allodynia (to light touch and/or deep pressure and/or joint movement)	
Vasomotor: evidence of temperature asymmetry and/or skin color changes and/or asymmetry	
Sudomotor/edema: evidence of edema and/or sweating changes and/or asymmetry	
Motor/Trophic: evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (nails, hair, skin)	
SCORE	