



# Percutaneous Management of Cancer Pain

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## Abstract

**Purpose of Review** To describe several effective imaging-guided, minimally invasive treatments to relieve cancer-associated pain in oncologic patients. Clinical applications, technical considerations, and current controversies are addressed.

**Recent Findings** The great variability in tumor subtype, location, and growth rates dictate the necessity for a tailored treatment approach. While opioids and radiotherapy may provide adequate relief for some patients, alternative minimally invasive procedures may augment these more traditional treatments or even provide superior palliative relief. Recent image-guided percutaneous techniques applied to reduce cancer-associated pain and minimize opioid dependence include neurolysis, ablation, high intensity focused ultrasound, and bone consolidation. Each technique treats cancer pain in a unique method.

**Summary** Minimally invasive interventional radiology techniques can provide effective and lasting pain palliation for cancer patients through both indirect and direct effects. Selection among treatments techniques should be based upon an individually tailored approach, to include consideration of all treatment modalities.

**Keywords** Pain · Oncology · Ablation · Neurolysis · Bone consolidation

## Introduction

Cancer-associated pain can be a source of significant emotional and physical burden that can affect quality of life and daily activities. While it is estimated that more than half of oncologic patients develop pain regardless of cancer type and stage, prevalence of cancer-associated pain is greater in patients with advanced disease stages and with certain tumor types including head and neck, lung, and breast cancers [1,

2]. Pain may be a result of direct tissue damage (nociceptive) or a result of dysfunction or damage to the nervous system (neuropathic). Despite the burden on quality of life, the majority of symptomatic patients (56% to 82.3%) remain undertreated [1], which may in part be related to access limitations for effective treatment options.

The traditional therapies for cancer pain can be generalized as conservative analgesic therapy [provided according to the World Health Organization (WHO) scale of analgesics], surgery, and radiation therapy. Each categorical treatment possesses strengths and weaknesses. Opioid administration requires the least amount of technical expertise and is effective for generalized pain relief. Limitations to opioid treatment include financial and public health concerns related to refractory pain relief requiring frequent medication usage and potential opioid dependence, systemic side effects that affect daily activities and mentation, and absence of treatment for the underlying pain stimulus [3]. Surgical resection of a tumor-causing pain may provide a more tailored approach to painful stimulus; however, cancer patients may present with contraindications to resection that include age-related comorbidities, advanced tumor stage precluding major interventions, and potential for surgery to delay systemic chemotherapy or immunotherapy. Radiation therapy provides a minimally invasive localized treatment option that may be very appealing

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for patients and providers; however, limitations include radiation dose constraints due to concern for iatrogenic induced sarcoma and blood born cancers, skin and muscular damage resulting in new pain, and overall moderate pain response that can be variable depending on tumor type, size, and location, and subtype [4].

Over the last few decades, a new, broad category of palliative care therapies has been introduced into the cancer pain management armamentarium. These minimally invasive techniques are made possible by advancements in imaging techniques, the development of low-profile technologies, and are utilized by interventional radiology practitioners who are skilled at performing the gamut of image-guided interventions. Each technique applies highly advanced imaging (e.g., computed tomography, magnetic resonance imaging) to guide treatment to directly or indirectly target the tumor that results in the painful stimulus. Each technique described herein (e.g., neurolysis, ablation, high intensity focused ultrasound, and bone consolidation) treats cancer pain in a unique method by destroying tumor stimuli, limiting stimuli from regional nerves, or stabilizing osseous structures to overcome mechanical pain [5, 6]. Limitations for these techniques include poor patient access, due to high-level specialization and procedural skill required, a limited overall awareness of these treatment strategies, and an unclear understanding by oncologists with regards to the how effective these therapies can be in treating cancer pain.

The purpose of this article is to describe several imaging-guided, minimally invasive techniques that are performed by interventional radiologists for pain relief in symptomatic oncologic patients. Clinical applications, technical considerations, and current controversies are reviewed.

## Percutaneous Neurolysis

Percutaneous neurolysis (PN) is a pain alleviation technique that aims to interrupt the pain signal transmission by the autonomous nervous system, specifically the sympathetic plexus [7•]. In cancer patients, the primary indication is to control visceral pain that is refractory to opioid therapy to improve quality of life and decrease opioid dependence [8]. The treatments can be applied for symptoms related to primary and metastatic tumor extension through visceral organs, or for pain that has been associated as a side effect of systemic therapies [9–11]. The most common location for treatment is the celiac plexus and splanchnic nerves [12], with current guidelines to support the procedure for tumor invasion into the bowel and visceral organs including the pancreas [13]. The palliative pain relief is achieved through the targeted degeneration of the sympathetic nerve fibers and ganglia via percutaneous thermal ablation or percutaneous injection

of a neurolytic chemical agent (Fig. 1). Both chemical and thermal ablation techniques are performed by the image-guided advancement of small caliber needles to the sympathetic ganglia.

## Chemical Neurolysis

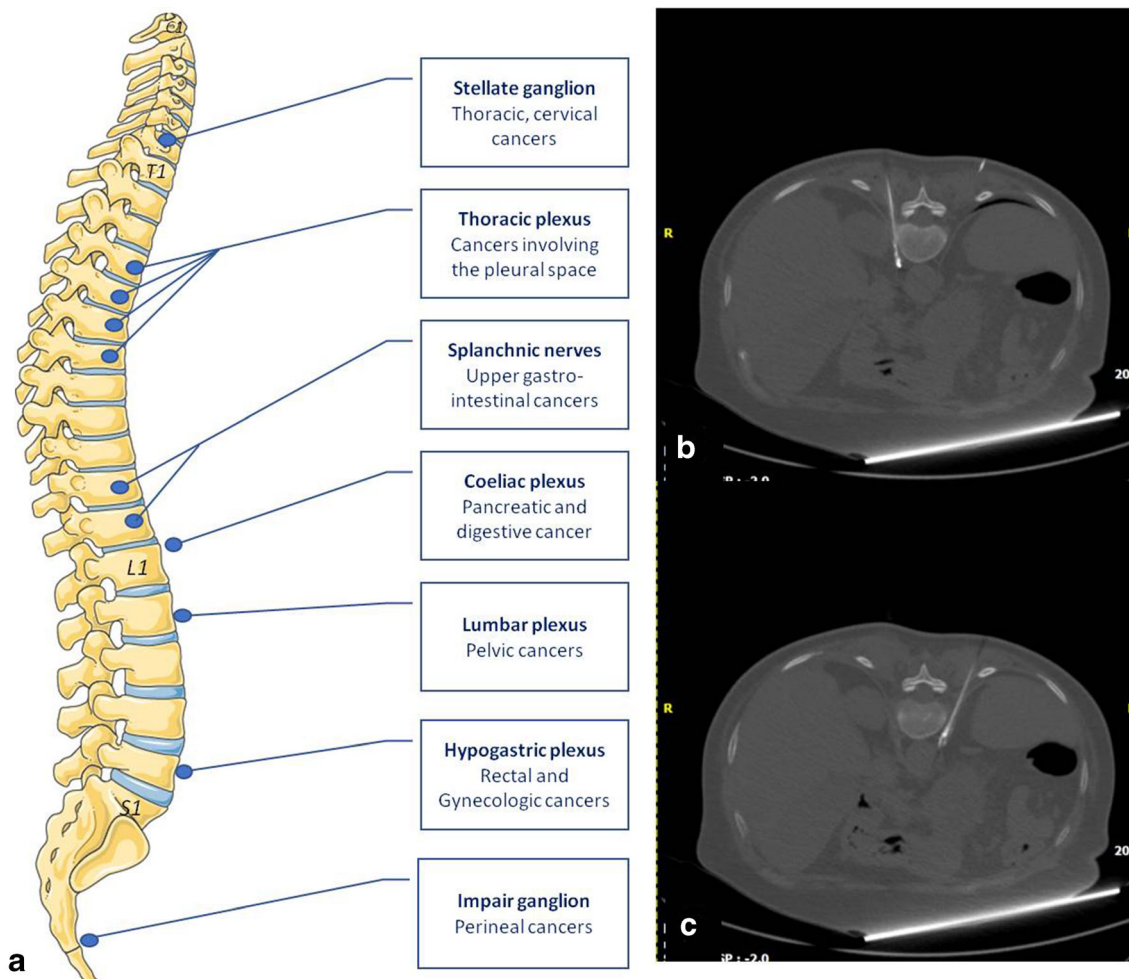
Chemical neurolysis is performed through the image-guided advancement of a 21 or 22 Gauge needle to the sympathetic chain. Overall, consistent results can be expected regardless of needle approach, which include anterior trans-abdominal versus posterior paravertebral, and unilateral versus bilateral blocks. Once the needle is in place, gentle syringe aspiration and small volume contrast injection can confirm an extravascular needle tip position. An injection of anesthetic can further validate needle position, as well as decrease peri-procedural pain. Immediate chemical neurolysis is then achieved by injection of a small volume of absolute alcohol. Injection volume is typically between 10 and 20 mL [10]. After subsidence of immediate procedural pain from chemical neurolysis, a significant pain reduction can be expected in 70–90% of patients [11].

## Thermal Neurolysis

Thermal ablation has been recently advocated as an effective alternative to chemical neurolysis. The low-profile ablation needle is advanced under image guidance to the sympathetic ganglion, and the tip is then activated to apply a predetermined zone of cell destruction by either heat-based technology (radiofrequency or microwave energy) or the creation of a therapeutic ice ball (cryoablation). These technologies may be particularly appealing over chemical neurolysis when tumor bulk prevents diffusion of liquid chemical agents, or in cases refractory to chemical neurolysis. A randomized clinical trial comparing bilateral splanchnic nerve radiofrequency ablation at T10-T11 levels versus bilateral ethanol neurolysis at a single T11 level favored thermal ablation, which provided more immediate results in a higher proportion of patients with greater durability [14].

## Technical Considerations

Regardless of whether chemical or thermal ablation neurolysis is applied, the cornerstone of effective neurolysis is image guidance. During pre-procedure work up, a careful evaluation of cross-sectional imaging will identify visceral tumor involvement and exclude procedural contraindications or negative predictive factors such as bowel obstruction and vascular invasion. During the procedure, the proceduralist relies on high-quality imaging to precisely guide the treatment needle to the targeted location. Historically, neurolysis has been



**Fig. 1** **a** Potential levels of percutaneous neurolysis for cancer pain alleviation. **b, c** A 69-year-old female patient with pancreatic cancer treated with splanchnic nerve neurolysis for pain reduction;

radiofrequency electrodes were bilaterally placed under computed tomography anterolaterally to T11 vertebral body

performed under fluoroscopic guidance; however, the availability and access to CT and fluoroscopic cone beam CT have advanced cross-sectional imaging as the gold standard for both chemical neurolysis and ablation [10]. Cross-sectional imaging provides greater contrast, spatial, and anatomical resolution than standard fluoroscopy to improve needle placement and ensure optimal clinical outcome.

Successful application of neurolysis requires timely diagnosis and a conscientious approach to pain management. Early diagnosis and referral for treatment are important to improve palliative efficacy, which is less beneficial in end-stage disease [15]. Patients should be carefully evaluated for baseline pain. Depending on clinical assessment, general anesthesia may be arranged during the procedure to ensure patient comfort throughout the procedure and immediate post-procedure recovery, as neurolysis can temporarily exacerbate pain during the process of nerve degeneration. Lastly, appropriate expectations for treatments, potential for retreatment, and possible complications of

diarrhea and hypotension should be discussed with the patient and their family [2, 16].

### Bone Consolidation

Tumor destruction of bone can result in structural instability, fractures, or erosion of muscle attachments. Image guidance provides the opportunity to provide effective pain and stabilization via minimally invasive techniques that include vertebral augmentation, cementoplasty, and fixation by internally cemented screws. Vertebral augmentation and cementoplasty reinforce weakened or fractured bone by the injection of bone cement (typically polymethyl methacrylate—PMMA), which provides resistance to axial compressive forces. Fixation by internally cemented screws describes the placement of metallic screws or rods with concomitant injection of bone cement. The addition of metallic hardware provides resistance to

torque and tension biomechanical stresses to compliment the axial compression resistance provided by the cement.

### Vertebral Augmentation

Vertebral augmentation methods include vertebroplasty and kyphoplasty as well as percutaneous insertion of spine implants [17–19]. Both vertebroplasty and kyphoplasty require the careful passage of small caliber needles via a posterior approach into the fractured vertebral body (Fig. 2). In vertebroplasty, the palliative effect is achieved by cement injection that fills the weakened vertebral body to reinforce the bone and prevent further loss of vertebral body height. In kyphoplasty, an additional step is performed before the cement injection to attempt restoration of vertebral body height before cement injection. The most common techniques for vertebral body height restoration require advancement of an inflatable balloon catheter or other expandable device through the access needle with subsequent device deployment to elevate the collapsed superior vertebral body endplate. The application of vertebroplasty versus kyphoplasty often depends on multiple factors including operator experience, degree of vertebral body compression, and tumor extension into the posterior vertebral body. Regardless of the vertebral augmentation method applied, studies have demonstrated significant pain reduction, decreased analgesic use, and improvement in disability scores [20, 21]. The treatments are indicated for vertebral body fractures caused by either cancer-related osteopenia or pathologic fractures [22].

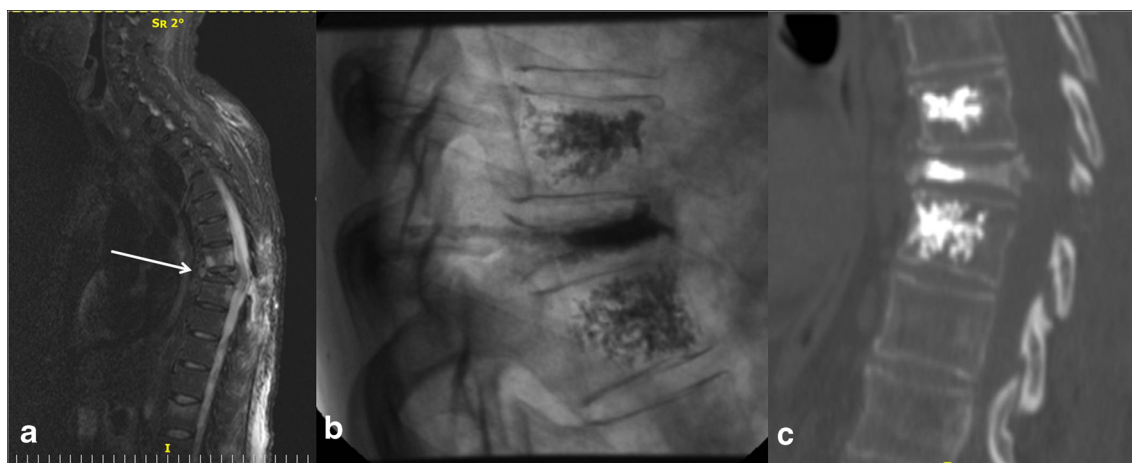
### Cementoplasty

Cementoplasty applies the same principles of vertebral augmentation to stabilize extra-spinal osseous structures

including the bony pelvis, ribs, and sternum [23, 24]. The technique is also known as percutaneous osteoplasty. The physical qualities of the bone cement are thought to provide pain relief through durable resistance to compression forces, adhesion of microfractures, and possibly exothermic destruction of nociceptive pain fibers that occurs during cement polymerization [25]. In addition to pain relief, cementoplasty can be applied as a preventative measure for impending pathological fractures [24, 26]. Similar to vertebral augmentation, the procedure can be scheduled in the outpatient setting. Durable pain palliation is expected in 1–2 days, once healing from the needle manipulation subsides [27, 28]. While cementoplasty can provide pain relief in osseous structures that bear axial weight, the procedure is less effective in bones subjected to torque stresses [29].

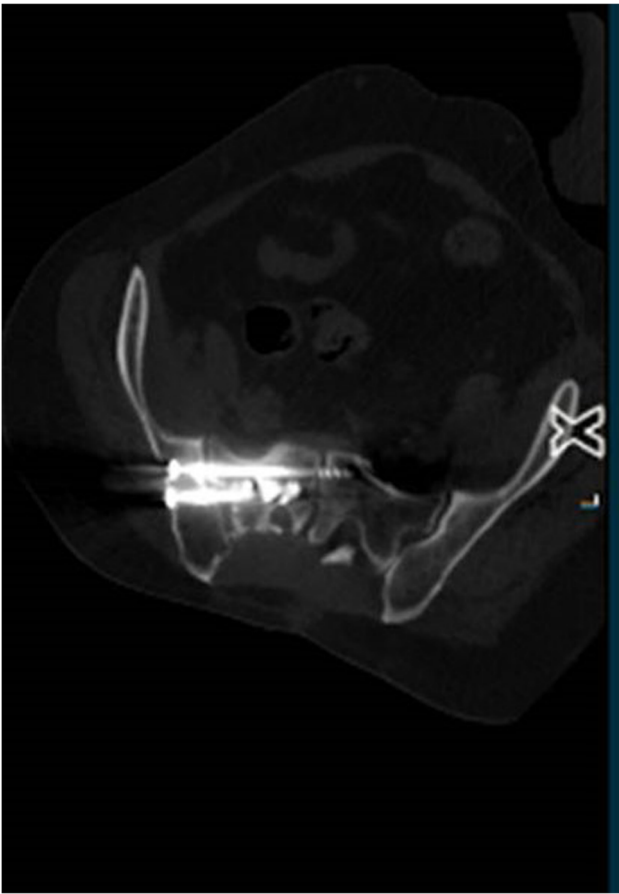
### Fixation by Internal Cemented Screw

Percutaneous fixation by internal cement screws provides an additional level of osseous reinforcement for metastatic bone disease that has extensively eroded a weight bearing bone. Advanced image guidance with navigation software and real-time tracking enables the operator to advance metallic screws or rods into the bone through 1–2-cm incisions. The hardware is subsequently anchored into the bone by cement (PMMA) consolidation [30, 31]. The addition of the metallic hardware confers a resistance to torque and tension stresses that complement the bone cement resistance to compression forces [32–36]. The most common utilization of FICS techniques is for pathologic fractures of the pelvis and femoral neck (Fig. 3) [37–41]. Effective FICS can be performed as a pain palliative procedure or as a preventative measure for an impending pathologic fracture [42].



**Fig. 2** A 60-year-old male patient with bronchogenic carcinoma and spinal metastatic disease was treated with percutaneous vertebroplasty post laminectomy and radiotherapy due to persistent pain. **a** Magnetic resonance imaging, STIR sequence depicting vertebral edema at T7,

T8, T9 levels; T8 vertebral body is illustrated with significant height reduction (white arrow). **b** Sagittal fluoroscopy view post cement injection in T7, T8, T9 levels. **c** Computed tomography sagittal reconstruction 24 h post vertebroplasty



**Fig. 3** Augmented sacroplasty with cement injection and cannulated screw insertion in a sarcoma patient with pathologic sacral fracture post radiotherapy

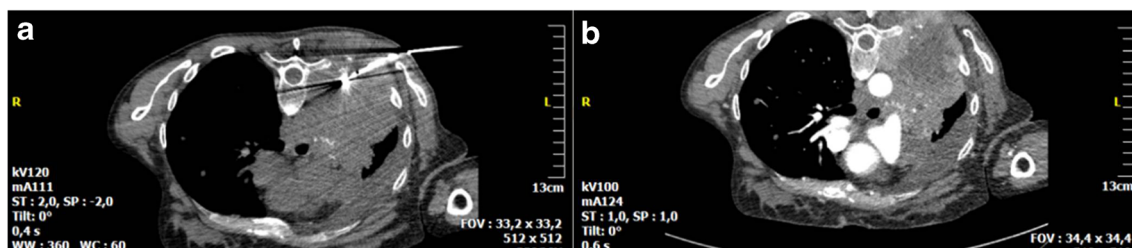
## Percutaneous Ablation

Imaging guided, percutaneous ablation either with high (radiofrequency, microwave, or laser) or with low (cryoablation) temperature techniques focuses on tumor destruction to significantly reduce pain up to 68–100% [42–56]. While thermal ablation is an effective stand-alone treatment, the treatment can also be combined with radiation therapy to improve the results [48, 49]. The pain palliative effect from thermal ablation results from necrosis of the interface between tumor and the pain-sensitive periosteum, decompression of tumor volume to relieve surrounding nerves and tissues, and reduction of tumor-induced cytokines to alleviate inflammation and nerve stimulation [42, 44]. Percutaneous ablation modalities include radiofrequency ablation (RFA), microwave ablation (MWA), cryoablation (CA), and laser ablation (LA) [43]. All modalities have proven pain palliative effects. Selection of the specific ablation technique takes into consideration operator experience and tumor histology, location, and size.

Percutaneous thermal ablation is performed by advancing small profile needle probes into the tumor and applying the thermal energy (Fig. 4). Each ablation modality provides treatment in a pre-defined zone of ablation. The procedures can be performed under local anesthetic or general anesthesia, depending on the modality, treatment location, and the patient's positional comfort. For tumor locations in close proximity to a critical structure such as a nerve or hollow organ, several thermoprotective techniques have been used to minimize complications. Active and passive thermoprotective techniques include thermal insulation with liquid or gas agent, as well as intraprocedural temperature and neurophysiological monitoring [45, 46]. Percutaneous ablation of bone and musculoskeletal lesions is as safe technique with a 2.5% rate of major complications more commonly associated with age greater than 70 years and use of more than three cryoprobes [57]. Ablation techniques in weight-bearing bones can be combined with bone consolidation techniques in order to provide structural support and avoid subsequent pathological fractures [47].

Numerous studies in the literature report the efficacy and safety of percutaneous ablation performed for curative intent in oligometastatic patients [58–61]. McMenomy et al. report post cryoablation a significant overall survival benefit that is governed by factors including size and number of metastases, length of disease-free interval, treatment adequacy of primary tumor, and presence of multiple metastatic sites [58]. Cazzato et al. report similar local progression-free survival rates among all the different tumor histologies and lesion size > 2 cm as a predictive factor for local tumor progression in a series of oligometastatic patients who underwent either radiofrequency or cryoablation [59]. Similarly, in a patient cohort undergoing radiofrequency or cryoablation sessions, Deschamps et al. report that good prognostic factors for local success include small-size (< 2 cm), lack of cortical erosion, and oligometastatic and/or metachronous diseases [60]. Recent studies suggest percutaneous ablation as an attractive alternative offering potential for complete remission in oligometastatic sarcoma patients [61].

As far as pain palliation is concerned, NCCN guidelines propose percutaneous ablation for adult cancer pain in cases of no oncologic emergency (e.g., pathologic fracture or epidural disease) of adequate pharmacologic therapy and/or radiation therapy contraindication or not desired by the patient [62]. Dupuy et al. applied radiofrequency ablation in previously radiated lesions with persistent pain; the authors report statistically significant pain reduction effect at 1 and 3 months of follow-up despite the fact that prior radiotherapy was not associated with significant pain reduction and mood improvement [63]. In a series of studies, Di Staso et al. reported that combining percutaneous



**Fig. 4** A 56-year-old female sarcoma patient with a large sized mass infiltrating thoracic wall and pain resistant to medication and radiotherapy. **a** Computed tomography axial scan illustrating the microwave antenna inside the mass close to the mass-thoracic wall

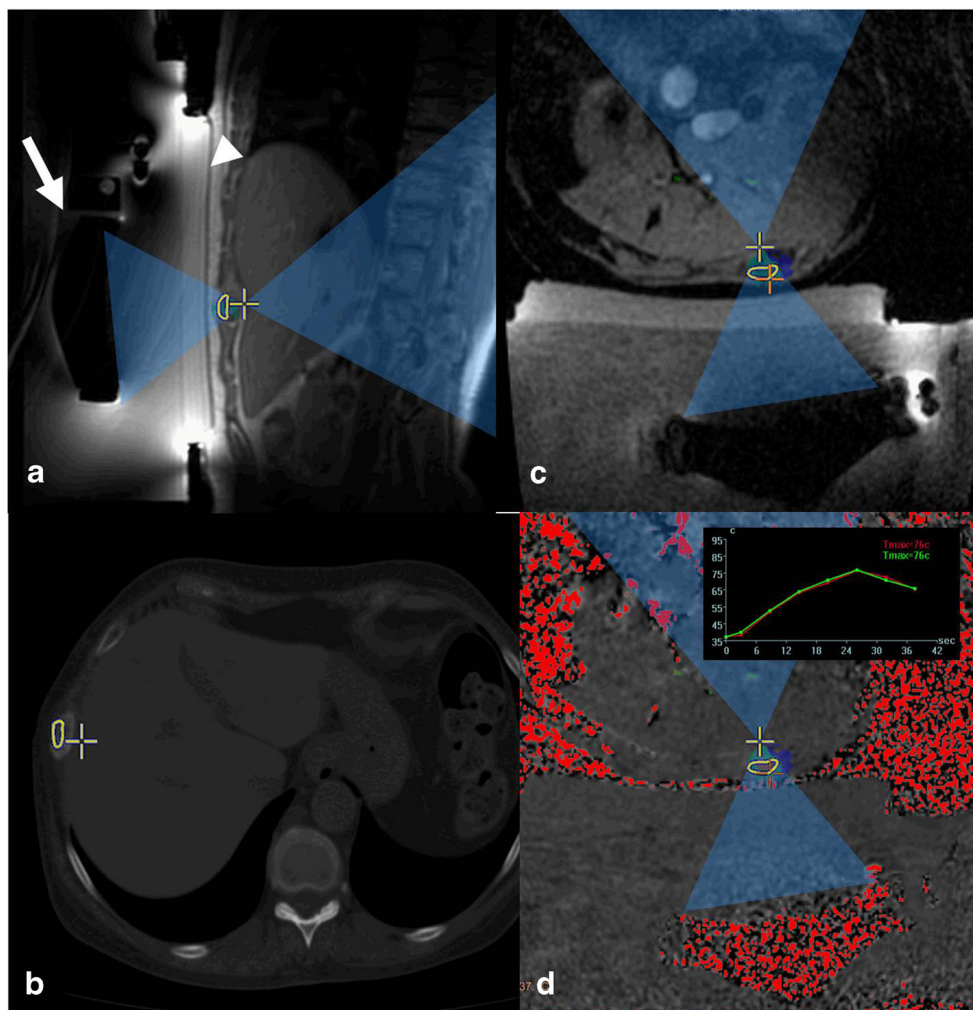
interface. **b** Computed tomography axial scan post intra-venous contrast medium injection illustrating the necrotic zone close to the mass-thoracic wall interface. There was significant self-reported pain reduction (> 70%) 1 week post ablation lasting for 9 months of follow-up

ablation (radiofrequency or cryoablation) and EBRT may act synergistically with no increase in the adverse event rate [49, 64]. Specifically, combined therapies resulted in significantly higher pain reduction effects earlier in the follow-up period, lasting for a longer duration of time and being associated with a more significant decrease in analgesics uptake [49, 64].

## High-Intensity-Focused Ultrasound

HIFU (high-intensity-focused ultrasound) is a noninvasive palliative option for the precise ablation of targeted lesions [65]. The technique is based on producing and focusing high-intensity ultrasound waves to deliver mechanical (thermal) energy on a location with no skin incisions or

**Fig. 5** Bone metastasis of a rib treated by MRgHIFU. **a** Sagittal view of the system with the HIFU transducer (white arrow), a gel pad (arrowhead), and the patient lying in lateral-oblique decubitus. The cross is the focus of the ultrasound beam, and the circle in the rib (lesion) is the targeted area of the selected sonication (area for energy delivery  $\geq$  ablation). **b** A pre-treatment CT is registered and fused showing the area of sonication in axial view. **c** Magnitude and **d** temperature map: images acquired during the sonication; at the end of the sonication, the area of expected ablation of current sonication is shown in green; the cumulative treated area including all previous sonications is shown in blue; in the box on the right, a graph shows the evolution of temperature at the target during sonication



punctures (Fig. 5). The improvement of symptoms may be immediate, and the procedure can be used in conjunction with chemotherapy and radiotherapy, to augment palliative effects. Procedural anesthesia is selected based on patient condition and positional comfort, and treatment can be performed in either the inpatient or outpatient setting [66].

HIFU acts upon different sources of cancer-related pain with a collective mechanism of action from both thermal and mechanical effects that include cavitation, microstreaming, and radiation force. The thermal effect is likely responsible for the greatest treatment effect, with neurolytic damage of nociceptive fibers to denervate the treatment area. The cavitation and acoustic pressure on tumors may also cause malfunction of membrane proteins, which alters ion interchange and membrane function, triggering variations on their electric transmission, with pain palliation achieved through neuromodulation [67, 68]. Lastly, fibrosis induced by ablation and shrinkage of the tumor mass reduces the regional mass effect and the degree of compression of adjacent nerve structures.

HIFU treatments are performed under ultrasound (USgHIFU) or MR (MRgHIFU) guidance [66]. Ultrasound guidance is less expensive and more widely available. During USgHIFU, the ablated area appears as hyperechoic spots; however, real-time monitoring of tissue temperature is not possible [67]. In comparison, MRI guidance offers greater anatomical resolution for pre-treatment planning, treatment monitoring, and assessment of post-treatment effects.

HIFU has proven effective for cancer-related pain in solid tissue organs and muscular metastases. Studies in symptomatic patients with pancreatic adenocarcinoma who underwent HIFU report significant (up to 81%) and long-lasting (up to 17 months) pain reduction effects [68–72]. Case reports of significant pain reduction post HIFU session include other neoplastic substrates such as pancreatic neuroendocrine tumors, hepatocellular carcinoma, abdominal lymph node metastases from gastric cancer, renal malignancies, and recurrent cervical cancer [73–79].

For bone metastases, HIFU achieves pain palliation through periosteal neurolysis by cortical heating [80–82], reduction of tumor size by coagulative necrosis, inhibition of osteoclast mediated osteolysis and skeletal remodeling, and accelerated sclerosis of osteolytic lesions [80–83]. Bone cancers can present a treatment challenge due to several factors. The relative low content of water in cortical bone and high-fat content of bone marrow preclude reliable temperature measurements and necessitate temperature extrapolation from the immediately adjacent soft tissue [83]. Furthermore, the difference in acoustic properties of bone and surrounding tissue results in heat dispersion that makes ablation of a subcortical lesion challenging and also consequently rises the safety profile [83]. HIFU can cause necrosis in the surrounding soft tissues or loss of functionality of joints due to transmission

of heat and bone damage or necrosis leading to fractures [66, 84]. Lastly, bone HIFU treatment can increase the fracture risk [82, 83], similar to percutaneous needle-guided ablation technologies. An understanding of these limitations ensures appropriate application of HIFU for specific bone tumors to optimize treatment outcome and minimize complication risks.

## Conclusion

Imaging-guided percutaneous techniques may act either indirectly or directly to provide significant pain alleviation and life quality improvement. Palliative treatment options include neurolysis, thermal ablation, bone consolidation, and high-intensity-focused ultrasound. Technical advantages of these procedures include the minimally invasive nature that can be performed in the outpatient setting or with a short hospitalization, low complication rates, little to no interruption of systemic chemotherapy agents, and ability to combine with other palliative treatment options. Advanced imaging and timely referral for pain palliation can optimize selection of the most appropriate technique in a patient-tailored approach to maximize efficacy of palliative pain relief.

## Compliance with Ethical Standards

**Conflict of Interest** Dimitrios K. Filippiadis, Lambros Tselikas, Alberto Bazzocchi, Evgenia Efthymiou, Alexis Kelekis, Steven Yevich declare they have no conflict of interest.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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