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On behalf of The Society of Interventional Oncology, we respectfully request the NCCN Bone Cancer Guideline Panel review the enclosed data for the following changes to be made to the NCCN Guidelines for Bone Cancer:

Background and Rationale for 2026 Petition

In April 2025, we submitted a petition requesting the addition of a "Principles of Image-Guided Tumor Ablation" section to the NCCN Bone Cancer Guidelines, analogous to the existing Principles of Radiation Therapy (BONE-C) and Principles of Pathology (BONE-D) sections. While ablation remains mentioned in limited contexts within the current guideline (CHOR-3, OSTEO-3, OSTEO-4, CHON-4), no dedicated principles section was added to the v2.2026 guideline published in December 2025.

However, a significant development occurred in March 2026: the NCCN Soft Tissue Sarcoma Guidelines (v3.2026) adopted a comprehensive "Principles of Interventional Oncology" section (SARC-F) that closely mirrors the language and structure we proposed in 2025 [1]. This section provides evidence-based recommendations for patient selection, ablation modality selection, contraindications, and site-specific considerations for liver, lung, and musculoskeletal metastases. Ablation and embolization procedures are now explicitly listed as treatment options across multiple STS algorithms for oligometastatic disease, recurrent disease, and palliative care [1].

Given the overlapping disease biology, metastatic patterns, and treatment paradigms between bone sarcomas and soft tissue sarcomas, we advocate for harmonization of the Bone Cancer Guidelines with the Soft Tissue Sarcoma Guidelines by adopting a similar Principles of Interventional Oncology section.

Specific Change Requested:

Include a **"Principles of Interventional Oncology" section (BONE-E)** in the NCCN Bone Cancer Guidelines, modeled on the SARC-F section from the Soft Tissue Sarcoma Guidelines, with bone-specific additions including:

- Thermal ablation (radiofrequency, microwave, cryoablation) for bone metastases and primary bone tumors
- Non-thermal ablation (irreversible electroporation) for lesions near critical structures
- Cement augmentation and osteosynthesis for weight-bearing bones with fracture risk

- Specific guidance for giant cell tumor of bone (GCTB), where cryoablation has established efficacy
- Emerging modalities (histotripsy) as clinical-trial-only options

New Evidence Supporting This Request:

1. Prospective Evidence for Radiofrequency Ablation (RFA) in Bone Metastases:

The **SPARTA Study** (Muto et al., 2026) represents the first prospective, multicenter trial specifically evaluating RFA for bone metastases [2]. Among 51 patients treated with RFA (78.4% followed by vertebroplasty), the study demonstrated:

- 100% technical success with no device-related adverse events
- Significant pain reduction at all time points: mean BPI score improvement of -3.3 at 1 month, -4.2 at 3 months, and -5.4 at 12 months (all p0.001)
- Sustained quality of life improvements through 12 months
- Level 3 prospective evidence supporting RFA as a minimally invasive treatment for painful bone metastases

This builds upon the OPuS One trial data (206 patients) showing rapid (within 3 days) and durable pain relief through 12 months, independent of radiation therapy [3-5]. A meta-analysis of 14 studies (426 patients) demonstrated median pain reduction of 67% over 24 weeks, with particular efficacy for axial lesions [6].

2. Cryoablation for Bone and Soft Tissue Sarcoma

Asanuma et al. (2024) reported local progression-free survival of **88.1% at 1 year and 79.7% at 2-3 years** for cryoablation of bone and soft tissue recurrences and metastases from sarcoma [7]. Histological examination confirmed complete necrosis in ablated areas. Risk factors for local progression included recurrent lesions after resection and lesions ≥4.0 cm.

A meta-analysis of cryosurgery for giant cell tumor of bone (38 studies, 1,373 patients) demonstrated a pooled local recurrence rate of only **13.5%** following cryosurgery, with low complication rates (3.9% fracture, 4.0% infection) [8]. Long-term follow-up studies show recurrence rates as low as 2.3% for primary GCTB treated with curettage and cryotherapy, with excellent functional outcomes in 92% of patients [9].

3. Combination Ablation and Structural Support

Setsu et al. (2025) demonstrated the feasibility of combining RFA with prophylactic intramedullary nailing for femoral metastases, achieving early pain relief, restored mobility, and significantly lower intraoperative blood loss compared to resection [10] Chlorogiannis et al. (2026) provided a comprehensive review confirming excellent local tumor control and pain palliation with thermal ablation combined with bone augmentation techniques [11].

4. Thermal Protection Techniques

Thurlow et al. (2025) published a detailed *RadioGraphics* review describing active and passive thermoprotective techniques critical to safe musculoskeletal ablation, positioning interventional oncology as "the fourth pillar of modern comprehensive cancer care." These techniques enable safe ablation near neurovascular structures and other critical anatomy [12].

Proposed Text for BONE-E: Principles of Interventional Oncology

General Principles

- Interventional oncology is positioned alongside surgery, systemic therapies, and radiation therapy as a component of modern comprehensive cancer care [12-14].
- Multidisciplinary team (MDT) discussion is required to assess the suitability and feasibility of interventional oncology approaches, to select the most appropriate technique, and to set the goals of treatment (i.e., curative or palliative) [1, 15].
- Interventional oncology techniques may be used alone or in combination with surgery, systemic therapy, and/or radiation therapy [13, 14].

Percutaneous Thermal Ablation

- Tumor ablation involves the application of FDA-approved thermal or non-thermal device therapies to a tumor to achieve cell death [1].
- Thermal ablation techniques include radiofrequency ablation (RFA), microwave ablation (MWA), cryoablation, and high-intensity focused ultrasound (HIFU) [15-17].
- Ablation modality should be based on tumor size, location, and adjacent critical structures to optimize treatment effect while limiting potential adverse events. Choice of modality may also take into account institutional experience and technique availability [1, 15].

Indications in bone cancer:

- Ablation (with or without embolization) is a treatment option for relapsed/refractory osteosarcoma when excision is not possible [18].
- Ablation is a treatment option for recurrent chordoma [18].
- Ablation may be considered for resectable pulmonary metastases from osteosarcoma when metastasectomy is not possible [18].

- Percutaneous ablation is an effective option for pain palliation in patients with painful osseous metastases or locally advanced bone tumors, including those refractory to or recurrent after radiation therapy [19-21].
- Percutaneous ablation can achieve local tumor control in the setting of oligometastatic disease [11, 22, 23].
- Cryoablation has demonstrated good local control for benign aggressive bone tumors (e.g., aneurysmal bone cysts, giant cell tumor of bone) and low-grade malignant bone tumors (e.g., borderline chondrosarcoma), with favorable functional outcomes compared to wide excision [24-26].
- Image-guided RFA is the standard treatment for osteoid osteoma, with higher rates of technical success, decreased morbidity, and lower cost compared to open surgery [19]. Cryoablation is a safe and effective alternative [24].

Patient selection:

- Patients with unresectable tumors or medical comorbidities prohibiting surgical resection could be considered for image-guided ablation [1].
- Patients whose disease progresses despite conventional therapies (chemotherapy, radiation) could also be considered for ablation [1, 23].
- Ablation for patients with painful musculoskeletal lesions may be combined with cement augmentation (osteoplasty), osteosynthesis, or internal fixation in the event of osseous destruction or increased fracture risk, especially in weight-bearing bones [1, 11, 14].

Contraindications:

Absolute contraindications to image-guided ablation include [1]:

- Uncorrectable coagulopathy
- Active infection in the planned treatment area
- Inability to displace or protect adjacent critical structures (relative, based on risk-benefit discussion)

Safety considerations:

- Thermal protection strategies (hydrodissection, pneumodissection, temperature monitoring, neurophysiologic monitoring) should be implemented to minimize the risk of undesired thermal injury to adjacent structures including skin, nerves, and bowel [12, 15, 21].
- Bone tumor cryoablation has a major complication rate of approximately 2.5%, with secondary fracture being the most common major complication [27].

Transarterial Embolization

- Transarterial embolization (TAE) involves the delivery of embolic agents within arteries supplying bone tumors with the goal of vessel stasis, inducing ischemic necrosis [28-30].
- Embolic agents include gelatin sponge particles, polyvinyl alcohol (PVA) particles, ethylene vinyl alcohol copolymer, and microspheres [28, 31, 32].

Indications in bone cancer:

- Serial embolization is a preferred treatment option (alongside denosumab) for giant cell tumor of bone (GCTB) that is resectable with unacceptable morbidity and/or unresectable axial lesions [18].
- Embolization combined with denosumab may have synergistic effects in promoting sclerosis and pain reduction for large sacropelvic GCTB [33, 34].
- Embolization is a treatment option for relapsed/refractory osteosarcoma [18].
- Serial selective arterial embolization (SAE) is an effective primary treatment for aneurysmal bone cysts (ABCs), particularly in surgically inaccessible locations (spine, pelvis), with healing rates of approximately 58%–83% and a lower complication rate compared to curettage and bone grafting [35, 36].
- Preoperative TAE of hypervascular bone tumors (including GCTB, ABC, metastatic renal cell carcinoma to bone, and other hypervascular tumors) reduces intraoperative blood loss, facilitates tumor resection, and may reduce transfusion requirements [32, 37-40].
- Preoperative embolization is particularly beneficial for tumors in the spine, sacrum, and pelvis where tourniquet application is not possible [28, 41].
- Preoperative embolization should ideally be performed within 24–48 hours prior to surgery to minimize revascularization [37, 38].
- Palliative TAE can achieve pain control in 60%–80% of patients with painful bone metastases, with a rapid median time to response of 1–2 days [41-43].
- TAE combined with radiation therapy may produce faster and longer-lasting pain relief than radiation therapy alone for painful bone metastases [44].

Patient selection:

- Multidisciplinary discussion should be performed to identify candidates who may benefit from embolization [15, 41].
- Embolization should be considered in the treatment algorithm where there is a high risk of bleeding at surgery, spinal involvement with neural encroachment, active bleeding, or in anatomically challenging surgical locations [28].

Contraindications:
Absolute contraindications include:

- Uncorrectable coagulopathy [1]
- Inability to safely catheterize the feeding artery
- Risk of non-target embolization to critical structures (e.g., spinal cord via radiculomedullary arteries) [41]

Safety considerations:

- Careful angiographic assessment is required to identify tumor feeding vessels and to avoid non-target embolization, particularly to the spinal cord and peripheral nerves [28, 31].
- Common adverse effects include transient local pain and post-embolization syndrome (pain, fever, nausea), which are generally self-limiting [41, 42].
- Serious complications are rare but may include skin necrosis, gluteal muscle necrosis, and nerve injury [35, 42].

Combined and Adjunctive Approaches

- Thermal ablation and transarterial embolization may be used in combination, with embolization performed prior to ablation to reduce tumor vascularity and heat-sink effect [13, 15].
- Ablation may be combined with osseous consolidation techniques (osteoplasty, vertebral augmentation, percutaneous screw fixation) to provide structural stabilization, particularly in weight-bearing bones at risk of pathologic fracture [11, 14, 23].
- These interventional oncology techniques can be readily combined with systemic therapies and radiation therapy as part of a multimodality treatment approach [13, 14, 22].

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Thank you for your consideration of these recommendations.

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