MSTS Metastatic Bone Disease Task Force, Part II

Submitted August 2024 by Felasfa Wodajo, on behalf of the MSTS Metastatic Bone Disease Task Force

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Top 8 Recommendations

- During fellowship training, fellows should achieve benchmarks related to management of MBD
- 2. Work together with the education committee to design a uniform curriculum to be taught to the fellows
- 3. Review every 5 years current recommendations of operative versus nonoperative management of metastatic disease
- 4. Post current recommendations for treatment of metastatic disease on the MSTS website, through the MSTS newsletters, and through AAOS periodicals
- 5. Form an "Industry Council" to serve as a liaison between industry and the society
- 6. <u>Via Industry Council, facilitate industry partnerships in areas adjacent to the medical and interventional management of MBD</u>
- 7. MSTS should establish two grants, one for basic science and other for clinical research in MBD
- 8. Identify and pursue potential funding sources for MBD grants

All Recommendations

Fellowships

- 1. <u>During fellowship training, fellows should achieve benchmarks related to management of MBD</u>
- 2. Work together with the education committee to design a uniform curriculum to be taught to the fellows
- 3. Consider inclusion of percutaneous pelvic stabilization as a recommended competency for fellows
- 4. Revise the case log requirements to match the distribution of cases in an orthopedic oncologist practice

Guidelines and Evidence Based Medicine

- 1. Review every 5 years current recommendations of operative versus nonoperative management of metastatic disease
- 2. Post current recommendations for treatment of metastatic disease on the MSTS website, through the MSTS newsletters, and through AAOS periodicals
- 3. Review every three years current recommendations regarding operative fixation versus resection and endoprosthetic reconstruction, etc.
- 4. Invite participation of members from adjacent specialty societies, i.e., medical oncology (ASCO), radiation oncology (ASTRO), ACS/SSO, and possibly patient members from the American Cancer Society (ACS) in the development of new clinical practice guidelines

Industry Partners

- 1. Form an "Industry Council" to serve as a liaison between industry and the society
- 2. Via Industry Council, facilitate industry partnerships in areas adjacent to the medical and interventional management of MBD
- 3. Partner with Industry for Radiofrequency Ablation Education
- 4. Partner with Implant Vendors
- 5. Partner with Companies that Specialize in Wound Dressings and Substitutes

Research

- 1. MSTS should establish two grants, one for basic science and other for clinical research in MBD
- 2. Identify and pursue potential funding sources for MBD grants
- 3. Poll Society membership to identify areas of focus for MBD research
- 4. <u>Establish MSTS mechanism for multi-institutional and/or multidisciplinary</u> studies

Introduction

Patients with metastatic bone disease (MBD) receive care by multiple specialists, often without one physician or specialty in charge, during this perilous portion of their cancer journey. As the leading national society for the study and treatment of musculoskeletal malignancies, the Musculoskeletal Tumor Society (MSTS) can and should take a more prominent role on behalf of this large patient population.

All MSTS members care for patients with metastatic disease, and many members are involved in basic and clinical research on MBD. The goal of the Metastatic Bone Disease Task Force (MBD Task Force) is to unify these strands into a strategic plan that will guide the MSTS towards a more prominent role on behalf of patients with metastatic bone disease. Thus, the Task Force is charged with developing a "road map" for the MSTS to follow in decision-making and resource allocation.

In 2023, Part I of the MBD Task Force report was submitted to the Executive Committee of the MSTS covering the following domains:

- 1. Annual Meeting
- 2. Disparities
- 3. Education
- 4. Novel Procedures
- Practice Management
- 6. Spine

In January 2024, the MBD Task Force began work again. With this second and final section of its report, the MBD Task Force completes its work and ends its tenure, leaving the selection and implementation of its recommendations to the Society and its leadership.

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Committees

As before, the work of the Task Force was performed in committees. For Part II, they were:

- Fellowships
- 2. Guidelines and Evidence Based Medicine
- 3. Industry Partnerships
- 4. Research

Each Task Force member served on two committees. With eight total members of the Task Force, there were four members per committee. As before, the Task Force was chaired by Felasfa Wodajo.

Committees scored each recommendation from 1 to 3 in terms of time to achieve and in difficulty. Thus, each recommendation is labeled as achievable in "1" – near term(< 2 years), "2" – intermediate (2-5 years) or "3" – long term (>5 years). Recommendations are also labeled to reflect the challenges and/or resources necessary to achieve the goal, as "1" – easily achievable, "2" – somewhat challenging or "3" – difficult.

Top Recommendations

Please note that in each of the sections below, the two "top" recommendations of each committee are separately indicated.

Committee Reports

Fellowships

Members:

- Daniel Lerman
- Jonathan Forsberg
- Howard Rosenthal
- Juan A. Pretell, lead

Background:

A Musculoskeletal Oncology Fellowship is a specialized training program for orthopedic surgeons who wish to focus on the diagnosis and treatment of musculoskeletal tumors. Provides advanced training to fellows, allowing them to become experts in the multidisciplinary care of patients with musculoskeletal tumors. During the fellowship, fellows are exposed to a wide variety of conditions including musculoskeletal metastatic disease, which is a significant portion of the curriculum. For this reason, it is important to make sure that adequate skills are learnt by the trainees so they can deliver optimal care to these patients in their practices.

Summary:

We believe as a group that musculoskeletal metastatic disease is a significant portion of our regular practice as orthopedic oncologists; therefore, it should be a priority during the training of our fellows. This should be focused on the multidisciplinary approach to their care, incorporating a homogeneous curriculum across the programs with emphasis on training in new techniques with less morbidity and taking in consideration the current extended expectancy of life.

Top Recommendations

Recommendation F1

During fellowship training, fellows should achieve benchmarks related to management of MBD

During fellowship training, the fellows should achieve different benchmarks related to exposure and management of MBD. Areas of interest should include:

- 1. Non-surgical management of spine, pelvic, and extremity MBD.
- 2. Surgical considerations and indications for MBD.
- 3. Multidisciplinary management of MBD, including:
- General knowledge of systemic treatments for carcinomas and sarcomas with MBD, and potential issues with surgical treatments.
- Indications/use of bone modifying agents.
- Understanding of radiation treatment options and timing with surgery.
- Minimally invasive techniques indication for ablation, AORIF, cementation, percutaneous fixation (including different implants available).

Timeline: 2 Difficulty: 1

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Recommendation F2

Work together with the education committee to design a uniform curriculum to be taught to the fellows

Work together with the education committee to design a uniform curriculum to be taught to the fellows. This could be done through Zoom presentations. To design this curriculum, there should be a subcommittee in charge of identifying the major areas of practice regarding MBD. Once these areas are identified, there should be topics delineated that should be approved by the program directors of the different fellowship programs. Fellowship program directors can be contacted by email/mail and a deadline will be defined for replying. In these topics, physicians from other specialties could be included based on relationship with the topic. All of this will be under the acceptance of the program directors.

Regarding the hands-on portion of the curriculum, this could be done through workshops during MSTS meeting, but also through coordination with industry partners – this will be in coordination with the MSTS Fellowship committee/ Education committee. The subcommittee that designed the lectures curriculum, should also identify major areas of interest for workshops, for example: Percutaneous stabilization of pelvic lesions, Technique for reconstruction with mega prosthesis, percutaneous ablation procedures, etc.

Timeline: 2 Difficulty: 3

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Other Recommendations

Recommendation F3

Consider inclusion of percutaneous pelvic stabilization as a recommended competency for fellows

Consider inclusion of percutaneous pelvic stabilization as a recommended competency for fellows. This would facilitate the dissemination of a novel and valuable surgical technique.

For programs who are not currently performing this intervention, it will take some time for the attending physicians to become educated on this intervention.

Time 2

Challenge 2

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Recommendation F4

Revise the case log requirements to match the distribution of cases in an orthopedic oncologist practice

Revise the case log requirements and incorporate procedures like percutaneous pelvic stabilization, and/or revise the number of procedures that will match the distribution of cases in an orthopedic oncologist practice (if needed to be revised).

Time 1

Challenge 2

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Guidelines and Evidence Based Medicine

Members:

- Jon Forsberg
- Alex Lazarides
- Dipak Ramkumar
- Yee-Cheen Doung, lead

Background

The treatment of metastatic disease has changed dramatically in the past 10 years with the advancement of targeted therapy including immunotherapy, tyrosine kinase inhibitors, germline-based inhibitors, etc. Because of these changes, life expectancy for patients with metastatic disease has increased. As a result, treatment plans are reflecting these changes.

Furthermore, the treatment of metastatic bone disease requires collaboration between medical oncology, radiation oncology, and surgery. Surgery is not always done by an orthopedic oncologist, especially in the setting of acute fracture. Most community orthopedists rely on what they have learned from training, what they see at meetings, and who they talk to in their community, to determine indications for surgery and type of surgery.

Top Recommendations

Recommendation G1

Review every 5 years current recommendations of operative versus nonoperative management of metastatic disease

Establishing standard of care treatment for MBD

The committee should consider a review every 5 years of

- -Current recommendations of operative versus nonoperative management of metastatic disease. Suggestions for evaluation of operative management include:
- -Current recommendations for operative fixation versus arthroplasty versus resection and endoprosthetic reconstruction
- -Current recommendations for intralesional curettage versus wide resection Suggestions for nonoperative management include:
- -Current targeted therapies and their potential perioperative interactions, including the role and timing of radiotherapy
- -Advances in palliative care management, including multimodal analgesic therapies and rehabilitation
- -Current interventional procedures like radiofrequency ablation and cryoablation

Difficulty: 1 or 2

Timeline: 1

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Recommendation G2

Post current recommendations for treatment of metastatic disease on the MSTS website, through the MSTS newsletters, and through AAOS periodicals

Disseminating knowledge and consensus opinion

- -Post current recommendations for treatment of metastatic disease on the MSTS website, through the MSTS newsletters, and through AAOS periodicals
- -target audiences include currently practicing orthopedic oncologists, orthopedic oncology fellows, orthopedic surgery residents, and general orthopedic surgeons who care for pathologic fractures.
- -ideally, can also disseminate this information to medical oncologists through ASCO and radiation oncologists through ASTRO
- -Provide MSTS sponsorship of Instructional Course Lecture and symposia at AAOS -have MSTS collaborate with other specialty societies (ASCO, ASTRO, American College of Surgeons (ACS) and/or Society of Surgical Oncology (SSO), possible patient members from the American Cancer Society(ACS)) to present current updates to clinical practice guidelines at meetings.
- -have MSTS collaborate with other specialty societies in developing new clinical practice guidelines, either through MSTS or through their societies.
- -Arrange "fast track" podium/posterior presentations or symposia at annual MSTS meetings for ASCO/ASTRO updates on the management of metastatic bone disease, and consider requesting reciprocal arrangements with other organizations.

Difficulty: 3 Timeline: 2 or 3

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Other Recommendations

Recommendation G3

Review every three years current recommendations regarding operative fixation versus resection and endoprosthetic reconstruction, etc.

Continuing Education for Orthopedic Oncologists and Orthopedic Surgeons

The committee should consider a review every three years of the following:

- 1. Current recommendations regarding operative fixation versus resection and endoprosthetic reconstruction
- 2. Current recommendations for operative and non-operative treatment of metastatic bone disease by primary histology and anatomic location
- 3. Current recommendations for intralesional versus marginal/wide resection and other interventional procedures (i.e., radiofrequency ablation, etc.)
- 4. Perioperative management (including drug holidays, assessment of perioperative interactions, etc.) of systemic therapies
- 5. Advances in post-operative management, including multimodal analgesic therapies and rehabilitation in patients with metastatic bone disease

Timeline: 3 Difficulty: 2

Recommendation G4

Invite participation of members from adjacent specialty societies, i.e., medical oncology (ASCO), radiation oncology (ASTRO), ACS/SSO, and possibly patient members from the American Cancer Society (ACS) in the development of new clinical practice guidelines

Inter-Society/Specialty Collaboration

- 1. Invite participation of members from adjacent specialty societies, i.e., medical oncology (ASCO), radiation oncology (ASTRO), ACS/SSO, and possibly patient members from the American Cancer Society (ACS) in the development of new clinical practice quidelines
- 2. Develop relations with these groups to be involved in the development of their clinical practice guidelines.
- 3. Arrange "fast track" podium/poster presentations or even symposia at annual MSTS meetings for ASCO/ASTRO updates on the management of metastatic bone disease, and request reciprocal arrangements with other organizations.

Timeline: 3 Difficulty: 3

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Industry Partners

Members:

- Alexander Christ
- Howard Rosenthal
- Daniel Lerman, Dipak Ramkumar, leads

Background

There are an estimated 400,000 new cases of metastatic bone disease (MBD) in the United States annually (Siegel, 2017). Historically, the management of MBD was responsible for approximately 17% of the cost of cancer care (Schulman, 2007).

Advances in the systemic therapy of metastatic carcinoma have resulted in an increasing prevalence of MBD and a growing population of long-term survivors living with the sequela of MBD and aggressive oncologic care. This population represents a new and ever-evolving clinical challenge. The orthopedic oncology community has a growing responsibility to support MBD patients through the utilization and development of multidisciplinary management to help maintain patients' quality of life throughout the duration of their newly realized longevity.

The MSTS membership should be well-versed in available pharmaceutical agents and procedures for aggressive MBD. The biomedical industry would benefit from our

membership's input to develop clinical goals, educational materials, and products. A great opportunity exists for a mutually beneficial relationship between our society and MBD-related industry partners.

Top Recommendations

Recommendation IP1

Form an "industry council" to serve as a liaison between industry and the society

Connect with relevant companies in the pharmaceutical and medical device industry that have products directly related to the treatment of metastatic bone disease. Ideally, this could be done through a specialized task force like an "industry council" that would be composed of member volunteers with representation from society leadership, to serve as a liaison between industry and the society. This council could help develop opportunities to include membership education and as well as opportunities for collaboration in research. The industry council should ideally represent the interests of the society as a whole and the patient population that we treat, and thus can potentially help dispel any concerns related to conflicts of interest from industry relationships specific to individual members.

For instance, bone modifying agents (BMAs) remain a cornerstone in the management of metastatic bone disease. Therefore, the MSTS membership should be well-versed in their indications, side effects, and benefits. Consideration for future directions could include local application of BMAs during procedures used for skeletal stabilization or treatment of MBD. Additionally, novel agents targeting newer pathways like sclerostin (romosozumab, Amgen) could also be investigated through industry-supported clinical trials at member institutions. Example pharmaceutical industry partners could include Amgen (Prolia, Xgeva, Evenity) and Novartis (Reclast, Zometa).

Similarly, this industry council can also explore opportunities with existing medical device companies to develop implants with specific applications in the treatment of MBD and osteoporotic/fragility fracture treatment population, including newer entrants like IlluminOss (photodynamic nails) and OsteoCentric (fenestrated and mechanically integrated screws). While the costs and resources needed for the development of MBD-specific implants may be prohibitive, the potential cross-application of these technologies in the fragility fracture population can certainly expand the potential patient population for the utilization of these new technologies. Thus, it is critical for the society to continue to collaborate with medical device companies (i.e., Onkos, Zimmer Biomet, Depuy Synthes, and Stryker) in the domains of educational opportunities, research, product development, and society support, and these responsibilities could be overseen by the industry council.

Lastly, it is also important to incorporate more novel interventional treatment approaches in the management of MBD. Newer studies have demonstrated the potential role of ablation procedures in the palliation of pain and potentially for local control in the treatment of MBD. Modalities including microwave ablation, cryotherapy, and radiofrequency (RF) ablation have been utilized by many interventional specialists in the treatment of MBD in the axial and appendicular skeletons. For multiple reasons, including procedural time, safety profile, and ease of use, RF ablation has gained the most traction in orthopedic oncology. With the evolving evidence base for its utility, RF ablation has the potential to become a critical component in the interventional management of MBD, and as a result, should also remain a focus of the industry council. Currently, Medtronic and Stryker both have bone-specific RF ablation systems (i.e., OsteoCool, and Optablate, respectively). Specific projects could include hands-on training and educational courses, as well as involvement in iterative product development and clinical research.

Timeline: 2 Difficulty: 2

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Recommendation IP2

Via Industry Council, facilitate industry partnerships in areas adjacent to the medical and interventional management of MBD

The industry council proposed in IP1, can also serve the role of facilitating industry partnerships in areas immediately adjacent to the medical and interventional management of MBD. This can include partnerships with organizations specializing in the development of wound care products (3M/Solventum, Smith and Nephew, KCI), including specialized dressings, vacuum-assisted closure devices, dermal and skin substitute products, and hemostatic agents. A significant portion of the MBD patient population are often treated with immunosuppressive systemic therapy in addition to higher doses of palliative radiation, which may portend poor surgical wound healing. Secondary complications including surgical site infections and prosthetic joint infections in this patient population and potentiate poorer survival, due to need for systemic therapy holidays and potential surgical irrigation and debridement procedures. Thus, collaboration with industry partners in this space, especially with respect to education of newer generation wound closure products and dressings, could be very beneficial for the society membership. Further, several clinical and translational research opportunities also exists in this space, that could be further explored by the industry council.

Timeline: 1
Difficulty: 1

Other Recommendations

Recommendation IP3

Partner with Industry for Radiofrequency Ablation Education

There is increasing utilization, and recognition, of ablation procedures' role in multidisciplinary management of MBD. Our interventional radiology colleagues employ multiple modalities—microwave, cryotherapy, radiofrequency (RF) ablation. For multiple reasons (procedural time, safety profile, ease of use) RF is the most accessible modality for the orthopedic oncology community.

There are two primary industry partners in this space—Medtronic with OsteoCool and Stryker with Optablate. Medtronic is an active sponsor of MSTS meeting and our relationship with them should continue. Up to this point, Stryker has not targeting MSTS for marketing of their RF system, which in some ways in more capable than the competitors. The society should connect with Stryker regarding Optablate in order to see is a mutually beneficial relationship can be established.

Education opportunities could include technical demonstrations and hands-on training experiences.

Timeline: 2 Difficulty: 2

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Recommendation IP4

Partner with Implant Vendors

The society can explore opportunities with implant companies to develop implants with specialized applications for MBD. The society has a long history of receiving funding from, and partnering with, orthopedic implant companies. Therefore, it is unlikely that this yields new significant financial benefit for the society. Furthermore, the costs and resources required for implant development may be prohibitive for companies when considering investment in the MBD space.

However, MBD related products would likely have benefit for the osteoporotic population and the same implant has been shown to be beneficial in both populations (e.g., IlluminOss, fenestrated screw systems).

As a close industry partner, Onkos may be open to specific development projects around MBD. The large US implant companies (Synthes, Zimmer Biomet, Stryker) would be worth connecting with in order to open dialogue about specific needs around treatment MBD and its potential applications to larger patient population, such as osteoporotic fracture care.

Orthopedic implant companies are a potential resource for society funding, educational opportunities and product development.

Timeline: 3 Difficulty: 3

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Recommendation IP5

Partner with Companies that Specialize in Wound Dressings and Substitutes

The society can explore opportunities with industry partners that specialize in wound dressings and substitutes. We, as Orthopedic Oncologists, typically deal with difficult wounds due to radiation, geriatric population and immunosuppressive systemic therapy. There are various dressings available (e.g., Silverlon which has been approved for radiation burns), non-cellular skin substitutes. A potential exists for mutually beneficial relationship regarding education, possible research opportunities.

Timeline: 1
Difficulty: 1

References

- 1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA Cancer J Clin. 2019;69(1):7–34.
- 2. Schulman KL, Kohles J. Economic burden of metastatic bone disease in the US. Cancer 2007; 109(11):2334–2342.

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Research

Top Recommendations

Recommendation R1

MSTS should establish two grants, one for basic science and other for clinical research in MBD

MSTS should establish two grants (funding permitting) with focus on basic science and clinical research within the field of musculoskeletal metastatic disease. Grant amount will be evaluated and decided by the Finance Committee. Grant application scoring and awards will be completed by the Research Committee, in a similar fashion to the Sarcoma Strong grants.

Timeline: 1 Difficulty: 2

Recommendation R2

Identify and pursue potential funding sources for MBD grants

Identify and pursue potential funding sources for MBD grants. This may include NIH, DOD, orthopedic implant companies, pharmaceutical companies, and private donors.

Timeline: 2 Difficulty: 3

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Other Recommendations

Recommendation R3

Poll Society membership to identify areas of focus for MBD research

Use the society membership and expertise to identify specific areas of focus relevant to metastatic bone disease where further research may be most impactful. The MBDTF can develop and poll the MSTS membership regarding topics of interest of metastatic bone disease.

Timeline: 1 Difficulty: 1

Recommendation R4

Establish MSTS mechanism for multi-institutional and/or multidisciplinary studies

Identify research topics that would be best suited to multi-institutional and/or multidisciplinary (including radiation oncology and medical oncology) study, and establish a mechanism through MSTS to perform those studies.

Timeline: 3 Difficulty: 3

Appendix

Members, MBD Task Force, Part II

MSTS committee representatives

- 1. Fellowship Juan Pretell
- 2. Guidelines and EBM Yee-Chen Duong
- 3. Research Alex Christ

At large

- 1. Alex Lazarides
- 2. Daniel Lerman
- 3. Dipak Ramkumar
- 4. Jonathan A. Forsberg
- 5. Howard G. Rosenthal

Presidential Line representative

1. Rajiv Rajani, vice president

Committee Assignments Fellowships

- 1. Juan Pretell lead
- 2. Dan Lerman
- 3. Jon Forsberg
- 4. Howard Rosenthal

Guidelines and Evidence Based Medicine

- 1. Yee-Cheen Doung lead
- 2. Dipak Ramkumar
- 3. Alex Lazarides
- 4. Jon Forsberg

Industry Partners

- 1. Dan Lerman lead
- 2. Dipak Ramkumar
- 3. Howard Rosenthal
- 4. Alex Christ

Research

- 1. Alex Christ lead
- 2. Juan Pretell
- 3. Alex Lazarides
- 4. Yee-Cheen Doung