

MSTS Newsletter

Volume 13, Summer 2013

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Are You Attending the 2013 MSTS Annual Meeting?

Mark your calendars for October 3 - 5, 2013, for the **2013 MSTS Annual Meeting** at the Hyatt Regency San Francisco. Program Chair Richard J. O'Donnell, MD, and President John H. Healey, MD, FACS worked with the Program Committee to select 60 podium presentations of the highest international caliber from amongst a record 185 abstract submissions. Session topics include aseptic and septic limb salvage complications; basic science advances; amputation, osseointegration, and rehabilitation; and humanitarian/collaborative efforts in orthopaedic oncology. Each session will include invited talks, papers of 3 to 7 minute length, and panel discussions. We will offer a robust Allied Health Program for Registered Nurses, Nurse Practitioners, Physicians'

Assistants, and Staff entitled "Innovations in Orthopaedic Oncology from A to Z" on Friday, October 4. We will conclude the meeting with James O. Johnston, MD, revealing our **"Tumor Unknown"** answers, with an iPad as the prize. Fees have been reduced this year to encourage participation and to afford attendees extra discretion in choosing from amongst the best in world-renowned Bay Area restaurants on Friday evening. Please register now at www.msts.org. **See you in San Francisco!**

Make Plans to Stay for the 2014 ORS Meeting

The Orthopaedic Research Society (ORS) meeting will start on Specialty Day and then follow the AAOS meeting. There will be two events with co-programming between the MSTS and ORS. On Specialty Day, **Best of the ORS** will be a basic science session featuring ORS presentations of relevance to the MSTS. On Sunday, there will be a joint workshop: **"Osteosarcoma: Future Directions in the Targeting of Micrometastases."** We are very pleased to be having this workshop and think this will be of interest and value to the ORS and MSTS membership. The workshop will be moderated by Kristy Weber, MD and clinical and basic science topics will be presented by Richard Terek, MD, John Healey, MD, FACS, and C. Parker Gibbs, MD in an effort to improve collaboration between clinicians and basic scientists.

President's Report - John H. Healey, MD, FACS

Although Chicago was cold, the hospitality was warm and the science was hot at the 2013 AAOS Annual Meeting and MSTS Specialty Day. The scientific program presented at Specialty Day was enhanced by international participants and major contributions from overseas. We hope that this is a harbinger of more international interaction and collaboration in scientific communication and inquiry. Oncology is now a global specialty. The MSTS will look for additional ways to foster these interactions, bringing international members to the USA and encouraging

American participation at international meetings. I will be representing the Society at the Japanese Orthopaedic Association in Hiroshima, the European Musculoskeletal Oncology Society in Göteborg, and International Society of Limb Salvage in Bologna. I encourage all of you to consider attendance at some or all of these outstanding society meetings. This way we can stay ahead of the information curve, learning of the latest developments when they are first presented, rather than waiting for the later publication.

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MSTS Executive Committee

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President's Report, cont'd from pg. 1

The MSTs official journal, Clinical Orthopaedics and Related Research (CORR), is off to a great start with the new Editor-in-Chief, Seth Leopold, MD. As I summarized in the President's Report at the Business Meeting in Chicago, there are many features important to our society. First, we continue to receive the journal as a complimentary benefit of affiliation. This is a concrete example of value added to the Society members from the CORR affiliation. The impact factor rose 20% last year to 2.53 (citations per article in the portion of two years covered by the survey). Several new features including Clinical Face-offs, editorial commentaries, Not the Last Word, and others are just some of the ways the journal has been revitalized and holds widespread value for our members who have Renaissance interests! The journal editorial support has also been reorganized. Our own Mark Gebhardt, MD has been elevated to the position of Senior Editor. In this capacity, he will be responsible for all of the tumor papers, will assign reviewers, and adjudicate issues with the Editor-in-Chief, Dr. Leopold. While he will have other responsibilities, tumor is his primary focus. We are lucky to have such an experienced, versatile, and knowledgeable person in charge. This is a great advantage for our society, authors, and oncology investigators. I will continue to be responsible for our MSTs Symposium generated from the best papers of the 2013 Annual Meeting. The Symposium has been of particularly high quality when our meeting was conjoined with other organizations such as ISOLS, CTOS, and EMSOS. We want to have

another top quality Symposium this year. This depends on our members presenting their top quality work at our meeting and completing their submissions PROMPTLY after the meeting. Having at least one of the twelve annual symposia in CORR is a great arrangement for our society since we comprise only 1-2% of orthopaedic surgeons. As always, we depend on the expert, timely reviews from members to assure the highest quality of peer review for the journal and our science. All interested reviewers should contact Dr. Mark Gebhardt, mgebhardt@bidmc.harvard.edu, Dr. Leopold, leopold@u.washington.edu, or myself, healeyj@mskcc.org. The relationship with CORR is win-win.

Finally, our society has made huge strides in our organization due to the structure imparted during Ed Cheng's Presidency and the implementation by our new management team (Jennifer Jones, CAE, Megan Lusk, Angie Schnepf, CAE, and Anna Greene, CPA, MBA). Again, I want to extend my deepest thanks for their efforts and the hard work of your Executive Committee members. Our Society is now on the firmest footing ever. The reports from each of the Committee Chairs will make this evident.

Most importantly the membership is growing in quantity and quality. There is a renewed interest in the Society by young and old members alike. Keep up the momentum! I appreciate your support during this year. See you in San Francisco.

President Elect's Report - Kristy M. Weber, MD

MSTs Strategic Planning Session after Annual Meeting

The MSTs Executive committee and staff have organized a strategic planning session to follow the Annual Meeting in San Francisco this October. A professional consultant has been hired to facilitate the process and focus on short and medium term goals of the Society with a focused plan to achieve those

goals. Representation from diverse groups within the society will be present. This summer, a Member Needs Survey will be emailed to all members soliciting your input about the future of MSTs. Please try to complete the survey so that we have your views represented.

Secretary's Report - Richard Terek, MD

I hope you enjoy the current edition of the MSTs newsletter and many thanks to those who contributed and to our production staff, Megan Lusk. The MSTs provides many opportunities for engagement with our specialty. Hopefully the newsletter will serve as a summary of the leadership's activities and a reminder of the many registration and application deadlines for our programs. To name a few: The Annual Meeting!, MSTs/OREF Clinical Research Award, Hatcher Fellowship, Clinician Scholar Development Program, Fellowship Match, Grant Writing Workshops, and MSTs Committees. It has been my pleasure to capture the goings on of the Society. Publication is every January and July. Contributions of interest to the membership are welcomed and may be forwarded to Megan Lusk at lusk@aaos.org. See you in San Francisco!

Editorial - Richard Terek, MD

Good news for musculoskeletal oncologists. We have a new addition to our armamentarium for treatment of giant cell tumor of bone (GCT): denosumab (Xgeva®, Amgen Inc.)(1). Arguably orthopaedic oncologists are best positioned to perform the comprehensive evaluation and management of patients with giant cell tumor of bone. Who else can interpret imaging studies, develop a plausible differential diagnosis, decide on the need for a biopsy, perform the biopsy, determine risk of pathological fracture, perform the surgical and adjuvant treatment, assess morbidity of surgical resection, assess for progression or regression both clinically and radiologically, assess impact upon adjacent joint function, assess for drug toxicity, and perform long term follow-up surveillance visits? Although current practice is to refer patients to medical oncologists for systemic treatments, in the old days, surgical oncologists administered their own chemotherapy and decided when the timing was right for surgery. Perhaps this paradigm will re-emerge for patients

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OREF/MSTS Clinical Research Grant Opportunity

The **Musculoskeletal Tumor Society (MSTS)** and the **Orthopaedic Research and Education Foundation (OREF)** invite clinical researchers to apply for an OREF/MSTS Clinical Research Grant in the area of clinical orthopaedic oncology as part of a grant sharing program. The PI or co-PI must be an MSTs member in good standing.

The objective of the grant is to encourage new and established investigators by providing seed and start-up funding for promising research projects that improve clinical outcomes for patients. Clinical relevance must be clearly noted in the abstract and specific aims, and be obvious from the title and the study design. Projects should be prospective, multi-institutional, if necessary, to meet accrual goals, and, if so, open to institutions of MSTs members.

Pilot studies should identify specific sources of potential longer term funding or matching funding. A total of \$100,000 is available. Maximum funding will be one grant of up to a total of \$100,000 over a one-to-two-year study period, conditional upon annual review for two-year studies. Projects for lesser amounts are eligible. Budget justification is necessary. Clinical projects are eligible, with clinical relevance explicitly and clearly described. Basic science proposals will not be considered (OREF has other funding mechanisms for basic science proposals). A list of MSTs research priorities follows, however other musculoskeletal oncology related topics will be considered. Applications will be available at: www.oref.org/grants. The application deadline is **September 12, 2013**.

MSTS Clinical Research Opportunities

- Randomized trial of Giant Cell Tumor of Bone treatment evaluating local and systemic adjuvants (e.g., cryosurgery, PMMA cement containing bisphosphonate, IV bisphosphonate, IV Denosumab)

- Randomized trial of Pigmented Villonodular Synovitis treatment evaluating open versus arthroscopic synovectomy and role of radiation therapy
- Randomized trial comparing clinical outcome of site specific bone metastatic lesions treated by internal fixation alone or with intralesional excision and PMMA cementation
- Randomized trial comparing endoprosthetic reconstruction with internal fixation of proximal femur metastatic disease
- Randomized trial comparing local recurrence of desmoid tumors after excision with and without radiation therapy

Priorities for research funding include prospective trial design comparing clinical outcomes for: proximal femoral replacement versus internal fixation for metastatic bone lesions to the proximal femur; Giant Cell Tumor of Bone treatment evaluating local and systemic adjuvants (e.g., cryosurgery, PMMA cement containing bisphosphonate, IV bisphosphonate, IV Denosumab); site specific bone metastatic lesions treated by internal fixation alone or with intralesional excision and PMMA cementation; local recurrence of desmoid tumors after excision with and without radiation therapy; Pigmented Villonodular Synovitis treatment evaluating open versus arthroscopic synovectomy and role of radiation therapy; expandable prostheses in children; press fit versus cemented stems for proximal and distal femur endoprosthesis; prospective observational study for computer navigation for pelvic tumor resections.

There is also discussion about developing an MSTs complication registry and/or developing a new system to improve margin assessment. Interested in discussing? Please contact me.

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Fellowship Committee – Robert H. Quinn, MD

Welcome, Tom Temple, MD, and Kurt Weiss, MD, to the Fellowship Committee! Thanks to Dempsey Springfield, MD, and Mark Scarborough, MD, for many years of service on the committee.

The 2013 Match has concluded. Thirteen of nineteen positions offered this year filled through the match process. Detailed match data and post-match survey results are pending.

Timeline for the 2014 Match:

- **June 1 – July 1, 2013:**
Update program information with SF Match. New programs submit applications through AAHKS/MSTS and (once approved) SF Match.
- **August 1, 2013:**
SF Match begins accepting requests for applicant registration.
- **September 16, 2013 through March 29, 2014:**
Programs will interview those applicants they select.
- **April 11, 2014:**
Rank list from programs and residents due to SF Match
- **April 25, 2014:**
Match Day.
Match Results Released.
- **April 28, 2014:**
Unmatched programs posted on SF Match website

The Hatcher Pathology Fellowship was acquired by the MSTs from the AOA in 2010. Details of the Fellowship as well as the application process have been recently defined and are available on the [MSTS website](http://www.msts.org). Applications will be accepted annually prior to the July 1 deadline.

Detailed **MSTS Curriculum Guidelines** for Clinical Fellowship Programs in Musculoskeletal Oncology have been approved by the Executive Committee and are available on the website.

MSTS Funded Projects

1. The Prophylactic Antibiotic Regimens in Tumor Surgery (PARITY): A Pilot Randomized Multi-Center Clinical Trial

is up and running. The PI is Michelle Ghert and is coordinated by the Center for Evidence-Based Orthopaedics at McMaster University. The trial is an international, multi-center randomized double-blind surgical trial in which patients undergoing endoprosthetic reconstruction of the lower extremity are randomized to either short-term (24 hours) or long-term (5 days) post-operative antibiotics. The primary endpoint is deep infection within the first year following implantation.

To date there are 17 active sites in Canada, the US and Argentina. Five further sites in the United Kingdom are in the start-up phase. Further interest has been expressed by several other sites in the US as well as sites in New Zealand, Japan, Israel, Scandinavia and South Africa. Funding for the PARITY study vanguard phase has been awarded by the OREF/MSTS, the Physician Services Incorporated Foundation and the Canadian Cancer Society. Currently there are 8 sites that are enrollment ready and screening patients. The first patient was randomized into PARITY in January 2013 and 13 patients have been randomized at the time of abstract preparation.

Interested in participating? Contact Michelle Ghert, MD via email at Michelle.Ghert@jcc.hhsc.ca, as all MSTS sponsored studies are open to all MSTS members.

2. **The ongoing MSTS CTra Fracture Prediction Prospective Study** continues to enroll patients in preparation for continued efforts at securing NIH funding. PI's are Brian Snyder, MD and Tim Damron, MD. Grant applications rely on continued enrollment of patients so all centers are asked to keep their IRB status current. Two papers currently in submission include one to Lancet, which summarizes the latest calculations of CTra sensitivity/specificity/accuracy compared to Mirels based upon the first 100 lesions with 3 month follow-up, and another evaluating the ability of CTra to affect physician decision-making derived from a survey format. A third manuscript in preparation will evaluate the durability of

the CTra prediction results compared to Mirels through 12 months follow-up. To date, over 150 lesions have been enrolled, and the project has yielded five published abstracts and six presentations at national and international meetings.

The MSTS congratulates and thanks all involved in supporting this multi-institutional prospective study through their efforts in financial support, patient enrollment, and participation. Anyone interested in participating in the study should contact Ara Nazarian, DrSc, anazaria@bidmc.harvard.edu, for more information.

The MSTS received three proposals submitted for funding this year, however none were approved. We hope that investigators revise and resubmit their applications. The grant workshops discussed below are one way to improve proposals. Thanks to all the applicants for their proposals and to the Research Committee for their intensive evaluations!

AAOS Clinician-Scholar Development Program

The 2014 **Clinician Scholar Development Program** (CSDP) will be **September 26-28, 2013** in Rosemont, Illinois. The program is open to residents, fellows, and junior faculty. The American Academy of Orthopaedic Surgeons (AAOS) selects some applicants and the MSTS supports up to two additional applicants with priority given to fellows and junior faculty. Our rationale is to cultivate talented individuals who will hopefully submit clinical trials to the MSTS or be involved in other scholarly and leadership activities.

Young Investigators Initiative Grant Mentoring and Career Development Program

The United States Bone and Joint Initiative (USBII) is dedicated to raising public awareness and to increase the research of musculoskeletal diseases. The Young Investigator Initiative is a career development and grant mentoring program that provides early-career investigators an opportunity to work with experienced researchers in our field to assist them in securing funding and other survival skills required for pursuing an

academic career. This career development and grant mentoring program is open to promising junior faculty, senior fellows or post-doctoral researchers nominated by their department or division chairs. It is also open to senior fellows or residents that are doing research and have a faculty appointment in place or confirmed. Basic and clinical investigators, with or without training awards (including K awards) are invited to apply. Investigators selected to take part in the program attend two workshops, 12-18 months apart, and work with faculty between workshops to develop their grant applications. This past spring Drs. Kevin Jones and Michael Monument from the University of Utah attended.

The **next workshop is November 8-10, 2013**, in Toronto, Ontario. The unique aspect of this program is the opportunity for attendees to maintain a relationship with a mentor until their application is funded. Application details can be found on the [USBII](http://USBII.org) website.

If you have any questions about the MSTS Research Committee or would like to discuss ideas you may have about research projects, please contact Lor Randall, MD at Lor.Randall@hci.utah.edu.

Treasurer's Report

- Ted W. Parsons, III, MD, FACS

I am pleased to report that the MSTS continues to perform quite well financially. We finished last year with assets exceeding \$720,000 including over half a million dollars in investments. With the considerable assistance from the AAOS staff, particularly Anna Greene, CPA, MBA, we have both successfully transitioned our financial records over to the AAOS and tightened up the financial reporting process for improved accountability. Additionally, with the assistance of Doug McDonald, MD (Membership Chair), we verified our membership records and have effectively dealt with many outstanding dues from years past. The society remains financially vibrant and growing, thanks to your engagement. We look forward to a successful 2013 and anticipate another financially rewarding year!

CPT Coding Committee – John P. Heiner, MD

The coding committee as we mentioned at the AAOS meeting, has had four topics of interest to our group.

1. The radical bone codes were reviewed in February at The AMA Relative Value committee (RUC) and were found to be in line with predicted Medicare expenses and were passed with no further review to be done. Therefore those RVU's are permanent.
2. The soft tissue codes (radical, subfascial and subcutaneous) did not follow Medicare's predicted usage and had site of service or diagnosis problems that we are trying to correct with revisions to the CPT book. Hopefully that will suffice. For now the RVU's for those codes will stay the same over the next three years; but they are at risk to be looked at in the future.
3. The primary total joint codes and the unicompartamental knee arthroplasty code were reviewed by the RUC in February and the surveys were problematic. The outcome at the RUC was not good and measures are being taken by the AAOS and AAHKS to see what we can do to affect the outcome. Over the summer it will become clearer if our efforts are having an effect.
4. ICD-10 comes out next fall (2014) in the U.S. Most large institutions have a conversion plan in place. Smaller offices probably have already looked at its effects but it is always a good idea to see what is coming. The WHO website can get you to ICD-10 and you can look at ICD-10 as it pertains to your practice and what documentation will be needed on your patients. The musculoskeletal portion for soft tissue sarcomas is not very specific but there is an opportunity to alter ICD-11 which is in the process of being built. Some of the benign entities can be found in several areas of ID-10 so it can be interesting (useful may be a better term than interesting) to go around the WHO website and look at where some of the codes are located.

Education Committee – Joe Benevenia, MD

- **2013 MSTS Annual Meeting**
October 3-5, 2013
San Francisco, CA
Chair: Richard J. O'Donnell, MD
Abstract Deadline: April 1st
Registration Deadline:
September 15th
Hotel Registration Deadline:
September 9th
[View the Annual Meeting Programs](#)
- **2014 AAOS Annual Meeting**
March 11-15, 2014
New Orleans, LA
Submission Deadlines:
 - ICL: May 1, 2013
 - Papers/Posters/Abstracts: June 1, 2013
 - Symposia: May 1, 2013
 - Scientific Exhibit: June 1, 2013
- **Specialty Day**
Date: March 15, 2014
Location: New Orleans, LA
Chair: Robert Quinn, MD
Co-Chair: Michelle Ghert, MD



AMERICAN ACADEMY OF
ORTHOPAEDIC SURGEONS

ORACLE

The AAOS Orthopaedic Research Assistance Center for Learning and Education (ORACLE) offers free research assistance to all AAOS members. ORACLE Services from the AAOS Library include: comprehensive literature searches, statistical data on musculoskeletal conditions and treatment, and general reference assistance. Typical requests are handled within five business days, but more involved projects can be scheduled accordingly. Submit requests any time via e-mail at oracle@aaos.org or by phone at (847) 384-4312.

We are not always able to respond to inquiries from non-members, so be sure to include your AAOS member number for the quickest response.

Information about ORACLE Services is available on the AAOS web site at <http://www.aaos.org/oracle>.

Editorial, cont'd from pg. 2

we see who have unresectable giant cell tumor. Now we can utilize denosumab either as long-term therapy or perhaps until there is healing and the tumor becomes resectable (2). Is there also a role for pretreatment of patients with tumors at higher risk of local recurrence? What about aneurysmal bone cysts? (3). Is it time for an MSTS sponsored trial on the treatment of GCT?

1. Thomas D, et al: Denosumab in patients with giant-cell tumour of bone: an open label, phase 2 study. *Lancet Oncol.* 2010 Mar; 11 (3):275
2. Branstetter DF, et al; Denosumab induces tumor reduction and bone formation in patients with giant-cell tumor of bone. *Clin Cancer Res.* 2012 Aug 15;18(16):4415.
3. Lange T et al: Denosumab: a potential new and innovative treatment option for aneurysmal bone cysts. *Eur Spine J.* 2013. Jun; 22(6):1417-22.

The views expressed here are solely those of the author and not those of the MSTS. Neither the author nor the MSTS endorse this product for on or off label use. Practitioners should review the full prescribing information.

FDA Approval for Denosumab

On June 13, 2013, the U. S. Food and Drug Administration approved denosumab (Xgeva® injection, for subcutaneous use, Amgen Inc.) for the treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity.

Denosumab's approval was based on demonstration of durable objective responses observed in two multicenter open label trials enrolling adult and skeletally mature adolescents with histologically confirmed, measurable giant cell tumor of bone. These tumors were either recurrent, unresectable, or were located where planned surgery was likely to result in severe morbidity. Patients received 120 mg denosumab subcutaneously every 4 weeks with

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Are You Interested in Volunteering for a MSTS Committee?

Visit the **NEW Volunteer Opportunities** page on the MSTS website! The Education Committee and the Research Committee are seeking volunteers for 2013-2016 **member-at-large** positions to be filled at the close of the 2013 MSTS Annual Meeting.

Apply Now!

The form will close on **August 19, 2013**. Questions? Email info@msts.org.

Editorial, cont'd from pg. 5

additional doses on days 8 and 15 of the first month.

A total of 304 patients received denosumab. The median age was 33 years (range: 13-83 years) and a total of 10 patients were skeletally mature adolescents (13-17 years). Radiographic assessments at baseline and following denosumab treatment were available for 187 (61%) patients. A retrospective determination of objective response was performed by an independent review committee using modified Response Evaluation Criteria in Solid Tumors (RECIST 1.1).

An objective response was identified in 47 of 187 patients for an overall response rate of 25% (95% CI: 19, 32). All responses were partial responses. The estimated median time to response was 3 months. In the 47 patients with an objective response, the median duration of follow-up was 20 months (range: 2- 44 months), and 51% (24/47) had responses lasting at least eight months. Three patients experienced disease progression following an objective response.

Safety data was evaluated in 304 patients with giant cell tumor of bone who

received at least one dose of denosumab. Of these patients, 145 were treated for at least one year. The most common adverse reactions were arthralgia, headache, nausea, back pain, fatigue, and pain in the extremity. The most common serious adverse reactions were osteonecrosis of the jaw and osteomyelitis.

The recommended dose and schedule of denosumab for the treatment of giant cell tumor of bone is 120 mg administered subcutaneously every four weeks with additional 120 mg doses on days 8 and 15 of the first month.

Full prescribing information is available http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/125320s094lbl.pdf.

Healthcare professionals should report all serious adverse events suspected to be associated with the use of any medicine and device to FDA's MedWatch Reporting System by completing a form online at <http://www.fda.gov/medwatch/report.htm>, by faxing (1-800-FDA-0178) or mailing the postage-paid address form provided online, or by telephone (1-800-FDA-1088).

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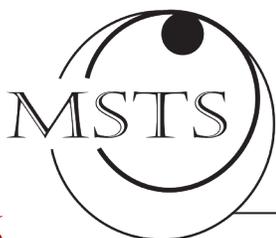
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