



2009 OTA Annual Meeting
Manchester Grand Hyatt
San Diego, CA

**(#F4) Clinical Research Seminar: Randomized
Controlled Trials**

America's Cup C/D, Level II

6:45am – 7:45am
Friday, October 9, 2009

Moderators: Mohit Bhandari, MD
Theodore Miclau, III, MD

Faculty: Michael J. Bosse, MD
Saam Morshed, MD
Emil H. Schemitsch, MD
Andrew H. Schmidt, MD

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Disclosure: Faculty disclosure can be found starting on page 67 of the 2009 OTA Annual Meeting program.

Clinical Research Seminar: Randomized Controlled Trials **Participating in Randomized Controlled Trials: How and Why**

Importance of Multi-Centre RCTs

- Orthopaedic trauma research has recently undergone a paradigm shift from single centre RCTs to larger multi-centre RCTs.
- A multi-centre trial is a collaborative effort in which more than one clinical centre is involved in enrolling and following study patients.
- The primary advantage of a multi-centre RCT over a single centre RCT is the ability to recruit more patients in a much quicker timeframe.
- Multi-centre RCTs also have the advantage of increased generalizability of the results. Typically, the more surgeons and the more clinical sites who participate, the more generalizable the results of the trial become.
- For multi-centre trials to be successful, collaboration across multiple sites and multiple surgeons is essential.

Multi-Centre RCTs in Orthopaedic Trauma

- Conducting a multi-centre RCT is a complex and time-consuming undertaking.
- A successful trial requires careful preparation addressing particular attention to writing a comprehensive protocol and identifying responsibilities of key personnel.
- A Methods or Coordinating Centre is a safeguard to promote standardization in a trial's methodology and a Methods Centre is critical in large, multi-centre trials. The Methods Centre coordinates all aspects of the day-to-day activities of the trial including communication with participating clinical sites, randomization, data management, and data analysis.
- It is vital that all participating clinical centres are adequately staffed by trained research personnel. The principal investigator at each clinical centre must be committed to collecting data in a uniform fashion and ensuring that the protocol is followed.
- The recently completed SPRINT trial is an example of a successful multi-centre RCT in orthopaedic trauma. The SPRINT study, which began patient enrollment in 2000, evaluated the effects of reamed versus unreamed intramedullary nailing on patients with tibial shaft fractures. This study included 1,339 patients from 29 clinical sites in North America and The Netherlands.
- Several research collaborative groups have been established with the mandate of completing multi-centre RCTs to definitively answer important clinical questions. Their successful collaborations have led to the completion of multiple high-quality RCTs.

Benefits of Participating in RCTs

- Individual reasons for participating in multi-centre RCTs may vary. There are multiple reasons to participate and benefits to collaboration. These include:
 - Answering important clinical research questions that will improve patient care.
 - Receiving authorship on resulting publications. Group authorship is usually used for publications from large collaborative RCTs. There is typically a Writing Committee that is responsible for preparing the publications. Authorship is often "The X Trial Investigators" with an appendix listing each collaborator's role.
 - Receiving academic merit and promotion.
 - Collaborating with experts and colleagues.
 - Improving knowledge about the disease and the treatment being investigated.
 - Possibly receiving exposure to new investigative techniques or access to special equipment or facilities.

Collaboration in Investigator Initiated RCTs

- There are many opportunities to participate in investigator-initiated RCTs. Investigator-initiated RCTs are usually pragmatic trials with little commercial interest.
- Many pre-established research groups may be looking for additional investigators to collaborate with them on investigator-initiated trials evaluating surgical procedures or techniques in orthopaedic trauma.
- These groups include:
 - The Canadian Orthopaedic Trauma Society (<http://cots.medicine.dal.ca/>)
 - The International Hip Fracture Research Collaborative (www.ihfrc.ca)
 - The Orthopaedic Trauma Research Consortium (www.orthotraumaresearch.com)
 - The South Eastern Fracture Consortium (<http://www.sefcf.org/>)

Participation in Industry Sponsored RCTs

- Another means of participating in clinical research is to participate in an industry sponsored trial.
- Pharmaceutical and device companies are often looking for qualified clinical sites to participate in regulatory trials where the sponsor is seeking approval to market a new product or approval of a new application for an existing product.
- Pharmaceutical trials may be financially lucrative; however, the requirements and workload may be demanding.

Things to Consider Before Agreeing to Participate in an RCT

- Participating in an RCT requires a substantial commitment of both time and effort.
- It is important to be sure that you are participating in an RCT that is right for you and your practice.
- The scientific, practical, and financial implications need to be considered before agreeing to participate in an RCT.
- The first item to assess is the study question and the study methodology. It is important to ensure that it is a relevant question and that the study methodology is sound.
- Next, it is important to assess the eligibility criteria to ensure that the clinical site treats a sufficient number of eligible patients to make participation worthwhile. The patient follow-up schedule and requirements should also be carefully assessed for feasibility.
- It is also important to assess the impact of the trial on your patients. It is necessary to consider whether patients will be required to have any investigations or procedures that are not part of standard care, and whether these will be painful and/or possibly put the patients at risk. One should estimate how much time the patient will devote to the study and how much, if any, compensation the patient may receive.
- The total costs associated with participating in the trial should be considered. In order to consider all costs, it is necessary to prepare an accurate budget for running the clinical trial at the clinical site. The budget should include research staff time, study supplies, expenses incurred by the patients, the cost of extra medical and hospital costs (i.e. pharmacy, radiology, and laboratory tests), additional physician time, and departmental and institutional overhead costs.
- It is necessary to ensure that qualified research staff are available to coordinate the day-to-day aspects of the RCT at the clinical site.
- It is also important to know whether the study will be published, who will write the manuscripts, and what the authorship policies are.
- After carefully weighing these items, one can make an informed decision about participating in the RCT.

Ongoing Multicenter RCT's in Trauma: Looking for You!

Andrew Schmidt, MD

- 1) Problems with multi-center clinical trials
 - a. IRB issues
 - b. Contracting issues
 - c. Support personnel
 - i. Research coordinator
 - ii. Clinic staff
 - iii. Resident
 - d. Time
 - e. Funding
 - f. Enrollment less than expected – often need more sites.

- 2) So you want to participate?
 - a. How is your IRB?
 - i. Costs
 - ii. How often do they meet?
 - b. Do you have the supporting personnel?
 - i. Research coordinator
 - ii. Research nurse
 - iii. Residents
 - c. Who can contract for you?
 - d. Obtain Human Subjects Research Training
 - i. Web-based sites
 1. <http://phrp.nihtraining.com/users/login.php>

- 3) How to get involved.
 - a. OTA Multi-center study group
 - i. IMPRESS
 - ii. SOLVED
 - iii. Ankle Fracture
 - iv. Others
 - v.
 - b. SouthEast Trauma Consortium
 - c.
 - d. Independent groups
 - i. LEAP
 - ii. FAITH/HEALTH
 - iii.
 - e. Be alert – pay attention!