

On the Reformation of Bioengineering in ISOLS

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Preface: I admire the wisdom and the far/hind sights of our Society President Peter Stedman for initiating this proposition. Most of the engineers entering into biology and medical fields were with immigrants' mentality not afraid of facing the new environment and dealing with unusual material properties and biophysical functions. More importantly, they were prepared with unequivocal determination to serve the medical community in an alternative and complementary role. I chose orthopedics and PM&R as my main medical fields owing to their close affinity with Mechanics and Materials. At Mayo, I was working with a team-effort minded colleagues helping me to learn and in solving clinical problems. I owe them for my career success and for chosen limb salvage as my main lifetime academic pursue. After more than four decades of working as a bioengineer, I have seen the rise and decline of this multidisciplinary endeavor, and never changed my enthusiasm and dedication to its purpose and objectivity. When Professor Stedman initiated this proposition and my colleague Frank Sim's strong endorsement, I did not hesitate to offer my service. This written report is to show my strong support and appreciation to the unprecedented and most timely call of action.

Reflecting on the past:

Formation of ISOLS - Before the formation of ISOLS, there were the Symposia on "Design and Application of Segmental Bone/Joint Replacement Prostheses" established in 1981 at the Mayo Clinic. These symposia were organized and held on a rotating basis in the American and European continents and the Asian Pacific region every other year. The main goals of the symposia were to share the design ideas and clinical application experiences of prosthetic implants including the use of autogenous bone and soft tissue transplants and allografts to preserve the limb and its function. Custom-designed and fabrication of implants for major revision cases preceded the idea of segmental bone/Joint implant development. In addition, the target patient population included those with bone and soft tissue malignancy, failed joint implants with massive bone loss, trauma and metabolic bone deficiency all could be benefited through limb salvage. Artificial limbs and external braces were also parts of the discussion contents. During that period of time, symposium participants had more bioengineers and material scientists presence. Industrial contributions were broader which drew support and interest from nearly all orthopedic device companies. After several rotations, the Symposium Board took the decision to form a more academic and attractive title to International Society of Limb Salvage (ISOLS). ISOLS went through its booming periods and members competed trying to host the general meeting for nearly three decades,

Contributions of Engineers in Limb Salvage - Bioengineers and material scientists worked with the surgeons in limb salvage were able to make many original and significant contributions for the improvement of limb salvage which also benefited the general orthopedic fields. The use of modularity design, hybrid stem fixation concepts, soft tissue direct attachment to implant, prosthesis surface coating, bone lengthening techniques, expandable implants, compression fixation to enhance initial stability of the implant-bone

junction, computer-aided preoperative planning, intraoperative navigation and postoperative rehab were just a few of such notable examples of ISOLS extraordinary achievements and productivity.

Custom-made Implant Successes and Problems: Early custom-made implants had borrowed the existing joint design concepts. The added advances in implant assembly and fixation techniques had significantly improved the surgery ease and the long-term prostheses and patient survival results. However, the articular surfaces after long period of use, revision became inevitable. The accumulation of wear particles created certain alarming side effects. Hybrid fixation made stem removal difficult in revision cases. With the 3D printing, molding and milling techniques available combined with rare metal coating, made the prosthesis price significantly increased, which added extra burden to the patients and the health care reimbursement agencies. In addition, implant quality control and assurance of long-term functional results were not established to justify their wide application. Soft tissue attachment directly and firmly attached to the metal implant still remains experimental. Finally, growing prostheses for young patients are impractical and troublesome. ISOLS members should all be duly concerned by these problems and working on their solutions as the main research challenge. Perhaps an alternative method of tumor ablation and eradication may offer conservative resection for more secured reconstruction combined with natural joint preservation technique would be the ideal limb salvage method in patients with musculoskeletal malignancy.

Decline of Bioengineers' Role in Limb Salvage: The decline of bioengineering as a vibrant research discipline for basic science and clinical applications in medicine was a general trend since the Millennium due to two major reasons. First, the rise of cell and molecular biology emphasis at NIH fueled by the advances in genome medicine had significantly shifted and diluted the research funding especially for relevant clinical investigations. Without NIH funding, many engineers had left their labs and some labs were dissolved or transformed to work primarily with the industry. The absence or degradation of rigorous lab testing and theoretical modeling had profound effects on the quality of clinician-engineer collaborative outcome. Secondly, physicians and surgeons are working directly with industry bypassing high quality and reliable investigation. Of course there were other reasons for the decline from the engineers' side. Such decline occurred earlier in ISOLS with decreasing bioengineering interest. This phenomenon was not entirely due to research funding decrease. Under President Stadman's reformation, we shall be able to address more on the questions of "What and Why" instead of "How" without strong evidence based on rigorous bioengineering analyses and experimental validation.

Current Interests and Project Ideas: I wish to yield the discussion on the current interests to my colleagues but dwell on the research ideas in my mind about limb salvage accumulated in the past three decades. In 1994, the application of Microwave (MW) hyperthermia for en bloc ablation of tumor mass and conservative reconstruction utilizing devitalized remaining bony structure as the graft scaffold for hybrid reconstruction caught my attention. Prof. QY Fan from China pioneered this technique. His long series of clinical results on the management of patients with aggressive benign and malignant bone tumors were impressive. I had been in the OR with him several times to witness the MW at work with hands-on experience. I also saw his lab tests and animal experiment data on the safety and efficacy issues of the hyperthermia technique in order to justify clinical trial studies. As

a member of ISOLS Board, I volunteered to organize and co-chaired with Sim & Fan two ISOLS workshops, 2015 in Gainesville, Florida and 2017 in Niigata, Japan. During these workshops, many problems and exciting prospects were discussed. From that, a host of new basic science research studies and animal experiments were proposed. In addition, multi-center clinical trials on benign aggressive bone tumor were also suggested. Unfortunately, Prof. Fan was facing with many difficulties related to the technology ownership, financial support, etc., which significantly hampered and limited the required R&D advances. However, I strongly believe that this technology has enormous potential in limb salvage field. With ISOLS encouragement, I was hoping that some of these experiments could have been conducted in simplified form as pilot studies to proof that microwave eradication of bone tumor mass is safe, effective and with high probability to draw further research support and industrial collaboration. I sincerely hope that with President Stedman's reformation initiative, the microwave technology and many other exciting innovations in limb salvage could be seriously and carefully reconsidered with the help of bioengineering modeling effort, lab testing and animal experiments.

Key Areas for Collaboration:

Although no laboratory facility was available to me since 2004, I wish to share the following study areas based on my own observation including that resolved from the two workshops on MW en bloc tumor ablation technology for ISOLS to consider, modify and put to action.

1. Lowering the cost of current custom-made prostheses;
2. Improving current modular segmental bone/joint replacement prosthesis design including the refinement of the initial implant fixation methods;
3. Soft tissue attachment to metal implant to improve limb function and implant in situ longevity;
4. Develop fixation system to be used after biophysical en bloc tumor ablation and hybrid reconstruction of the skeletal system;
5. Improving extendable implant and explore alternative limb salvage technique in young patients;
6. Explore the safety of hyperthermia (microwave energy) and hypothermia (cryosurgery) on the local and systemic control of bone and soft tissue malignancy;
7. Use of microwave in the treatment of aggressive benign bone tumor (i.e. Giant cell tumor) - both on biomechanical and clinical studies;
8. Investigate the potential of blood vessel and nerve preservation in the eradication fields using hyper or hypothermia energy to improve the outcome in patients with soft tissue malignancy;
9. Study the non-tumor related limb salvage problems and needs;
10. Improve exoskeleton attachment of artificial limb prosthetics;
11. Explore the possibility of biological joint preservation in limb salvage surgery;
12. Limb salvage problems of tumor in the spine;
13. The role of bone lengthening and transport in young limb salvage patients;
14. Shared successes and problems in Non-tumor related limb salvage experiences.

Steps and Project Timeline:

The 1st step of action would be for the ISOLS Board to announce and organize a formal discussion-based Forum in the Scientific Program in the coming Society Meeting in Vienna to kick off the reformation based on its importance and urgency. In the Forum, the summary and key points of the August Zoom Meeting summary will be the basic reference for the discussion. Appropriate sub-session leaders will be appointed to facilitate the interchange of opinions. In addition, the August Summary will be made available to the general membership so that they may be better prepared to play a part.

In order to encourage and support non-member engineers to attend the meeting, similar discount on the registration for the allied health professionals (nurses, rehab and other non-MD personnel) may be considered. The Board may discuss pilot study funding issues and other incentives programs including special awards to assure the success of the reformation. Individual, Society, Foundation and industry donated seed money program for new investigators will be discussed. The Board may designate members to provide research grant preparation assistance and guidance. During ISOLS meeting special topic session with bioengineering emphasis may give priority for podium presentation. In between meetings, webinars and zoom meetings concerning bioengineering research will be organized. The Society office will announce the collaborative research opportunities including funding to keep the reformation momentum going. Project timeline can only be discussed after the joined research projects are successfully established and the funding issues are resolved.

Forum Ideas for ISOLS-2026 in Vienna:

Based on the main goal of the reformation, the Forum may adapt the title of **“Bioengineering Attributes in Limb Preservation”**. Using the contents of the above section on “Key Collaborative Areas” the Forum may be organized into several sessions using the subject titles to be announced to attract members and their colleagues to submit abstracts for the Vienna meeting.

Epilog:

There are perhaps three main reasons to initiate this timely and exciting reform proposition: 1) To strengthen ISOLS as the elite multi-disciplinary academic Society; 2) To refine and optimize many of our innovative ideas through R&D collaboration; 3) To re-establish bioengineering as one of the pillars of orthopedics and the entire medicine and surgery fields. Orthopedic oncologists are well known to recruit and work with the talented counterparts in order to provide the best possible care to the patients. The limb salvage aspects require solutions that are effective, reliable, safe, and affordable. These are the fundamental requirements of the engineering and the medical professions. Therefore, the surgeon-engineer team seems ideal to deliver satisfactory results in limb salvage.

The call for reformation of biomedical engineering in ISOLS has a very special meaning and strong impact to those who worked hard to advance the field of “Orthopedic Biomechanics” and its basic science and clinical applications. During the heydays, engineers were admitted into AAOS as Associate Members, and with the privilege of serving on various committees. Although we had managed to solve problems, we also realized that these solutions were not perfect. New problems revolved demand solutions with or without improvisation.

Research is a continuous endeavor that requires constant supply of new energy, personnel and financial support. Furthermore, bioengineering has been regarded as a non-traditional medical basic science. When hard time came, decline of attention and emphasis would follow, which were expected. I do admire President Stedman's courage and wisdom in instigating this timely reformation based on the strong evidence of engineers' relevant contributions. Naturally, I was obligated to prepare this lengthy report to show my sincere appreciation. Hopefully, this report will aid him to revive bioengineering in ISOLS to rejuvenate its successes and attraction once enjoyed in the 80s, 90s and beyond.

I am sure all of you agree that there are many unsolved problems in limb salvage. They shall also bring immense opportunities. We need to do the right things through reform and move forward. No one expect that these could be achieved single-handedly nor within a fixed period, with the lasting teamwork spirit, these problems will be solved in due time within the life span of ISOLS. God speed to you all in your work, academic pursues and family life journeys!

Acknowledgement:

In my entire professional life, I had the fortune of joining several orthopedic related academic societies, but none could be compared to ISOLS and its predecessor, the Symposia in terms of honor and personal satisfaction. I do appreciate my colleagues accepting me with the confidence and trust in me to serve the role of General Secretary and on the Board of ISOLS. In retribution, I wish to pay my sincere gratitude to my mentor Jack Ivins who guided and coached me in getting our major NIH/NCR grant on limb Salvage which continuously been funded for 23 years with the meritorious status for the last five years. Another closest friend and partner at Mayo I must pay tribute to is Frank Sim. I owe him for his support and encouragement, which greatly motivated me to get into the clinically relevant work in and outside of Limb Salvage. Most importantly, he built confidence in me. Our bonding relationship may serve as a role model for future young investigators. The achievements I was lucky to have shared were also the tireless and dedicated work of the laboratory staff and the fellows/students at Mayo and Hopkins from all around the world. I am indebt to them for allowing me to see further by standing on their shoulders.

This lengthy report is a reflection and condensation of my lifetime work experience. I wish to dedicate it to our President Peter Stedman, my friend Frank Sim and the entire ISOLS membership. Your critique, addition, corrections and suggestions will be accepted sincerely from the bottom of my heart.

Respectively submitted by

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