EMPIR Call 2015 – Health, SI, Normative and Research Potential

Selected Research Topic number: **SRT- h20**
Version: 1.0

Title: Metrology for high intensity ultrasound treatment planning

Abstract

High intensity therapeutic ultrasound is a promising non-invasive, non-ionising extracorporeal beam therapy which selectively destroys pathogenic tissue and spares healthy tissue by focusing high-frequency, high-intensity sound waves to within a small volume. This therapy is rapidly gaining widespread clinical acceptance for treatment of prostate cancer and uterine fibroids. However, in order to advance its applicability in the treatment of deep-seated tumours and improve surgical outcomes, metrological tools for the verification and validation of treatment planning routines, such as computation reference standards, need to be developed. The availability of such tools will accelerate the development of therapeutic ultrasound.

Keywords

Treatment planning, computational reference standards, nonlinear acoustics, near-field acoustic holography, tissue mimicking phantoms, personalised medicine.

Background to the Metrological Challenges

High-intensity focused ultrasound is a promising extracorporeal beam therapy which seeks to selectively destroy pathogenic tissue by mechanical and thermal ablation, while sparing healthy tissue. It is non-invasive, non-ionising, and due to the nature of the focusing mechanism, it can accurately be targeted to destroy pathogenic tissue, while minimising damage to healthy tissue. Currently it has regulatory approval for the treatment of prostate cancer and uterine fibroids. However, in order to fully exploit the potential, there is a need to develop tools to facilitate the next generation of therapeutic devices which can be used to treat difficult locations, such as transcranial or trans-costal, for which resection is often not a viable option. Such applications require accurate treatment planning to focus the beam and deliver the intended dose.

The use of dose recipes and computational phantom are well established for radiotherapy treatment planning and adaptive treatment planning routines that are already entering the market. However, as therapeutic ultrasound is an emerging technology, such capabilities are not yet as advanced as those used in radiotherapy. For example, all the approved ultrasound clinical devices perform ray-tracing to target the beam and as such no treatment plan can be computed because no dose is calculated. Furthermore, ray-tracing disregards fundamental physical effects such as diffraction, absorption and nonlinearity; the only physical effect that can be included in such models is the correction for aberration. Consequently, those devices cannot be applied to deep seated tumours, neither accurately or reliably spare healthy tissue.

There are a number of factors which restrict the utility of treatment planning code: namely the computational requirements and the difficulties of ascertaining acoustic properties of tissue *in vivo*. Currently, cutting edge solvers, working at clinically relevant parameters, take many hours to run on distributed high-performance computing facilities.

Treatment planning software is classified as a medical device, and as such falls under the Medical Devices Directive, (specifically MDD 93/42/EEC, annex IX). Thus, in order to gain regulatory approval both validation and verification must be addressed. Current IEC guidelines only relate to quality systems (ISO/IEC 90003:2014) and life-cycle processes (IEC 62304:2006).

In order to compute the dose delivered, the acoustic field must also be computed. However, due to high frequency, large propagation distances and nonlinear wave propagation, computation of the acoustic field is computationally demanding. Furthermore, in contrast to radiotherapy, ultrasound significantly interacts with tissue requiring detailed knowledge of the acoustic properties of tissue in order to model propagation and to

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compute dose. Measuring the acoustic properties of tissue for clinically relevant frequencies and intensities is challenging and results have shown a wide spread, even for a single tissue type.

Objectives

Proposers should address the objectives stated below, which are based on the PRT submissions. Proposers may identify amendments to the objectives or choose to address a subset of them in order to maximise the overall impact, or address budgetary or scientific / technical constraints, but the reasons for this should be clearly stated in the protocol.

The JRP shall focus on the traceable measurement and characterisation of high intensity therapeutic ultrasound for treatment planning.

The specific objectives are

1. To establish an open-source hierarchy of computation phantoms to enable the comparison of computed acoustic fields and thermal fields from different groups as a means of validating treatment planning codes for high-intensity ultrasound;
2. To develop and validate improved methods for measuring clinically relevant tissue properties and provide numeric data for the computational phantoms;
3. To extend governing equations to better account for the effects of interfaces and local in-homogeneities so that a wide range of computation phantoms, including physically representative models, are modelled. In addition, to extend current capabilities of 3D nonlinear code to a high-performance computer cluster to improve speed and handling of large sized domains, relevant to treatment of deep seated tumours (e.g. over 10 cm in depth);
4. To modify the existing methods and develop new ones to experimentally validate treatment plans in a clinical setting based on appropriate phantoms using well-characterised tissue mimicking materials and 3D printing of bone phantoms;
5. To facilitate the take up of the technology and measurement infrastructure developed by the project by healthcare professionals (clinicians, etc.), standards developing organisations (IEC, Focused Ultrasound Foundation etc.) and industry (instrumentation manufacturers).

These objectives will require large-scale approaches that are beyond the capabilities of single National Metrology Institutes and Designated Institutes, and it is expected that multidisciplinary teams will be required. To enhance the impact of the research, the involvement of the appropriate user community such as medical practitioners, medical (academic) hospitals and industry is strongly recommended, both prior to and during methodology development.

Proposers should establish the current state of the art, and explain how their proposed project goes beyond this. In particular, proposers should outline the achievements of the EMRP project HLT03 (DUTy) ‘Dosimetry for ultrasound’ and how their proposal will build on those.

EURAMET expects the average EU Contribution for the selected JRPs in this TP to be 1.8M€, and has defined an upper limit of 2.1 M€ for this project.

EURAMET also expects the EU Contribution to the external funded partners to not exceed 35 % of the total EU Contribution to the project. Any deviation from this must be justified.

Any industrial partners that will receive significant benefit from the results of the proposed project are expected to be unfunded partners.

Potential Impact

Proposals must demonstrate adequate and appropriate participation/links to the “end user” community, describing how the project partners will engage with relevant communities during the project to facilitate knowledge transfer and accelerate the uptake of project outputs. Evidence of support from the “end user” community (e.g. letters of support) is also encouraged.

You should detail how your JRP results are going to:

- Address the SRT objectives and deliver solutions to the documented needs,
- Feed into the development of urgent documentary standards through appropriate standards bodies (e.g. IEC TC87),
- Transfer knowledge to the healthcare and industry sectors.

You should detail other impacts of your proposed JRP as specified in the document “Guide 4: Writing Joint Research Projects (JRPs)”.

You should also detail how your approach to realising the objectives will further the aim of EMPIR to develop a coherent approach at the European level in the field of metrology and include the best available contributions from across the metrology community. Specifically the opportunities for:

- improvement of the efficiency of use of available resources to better meet metrological needs and to assure the traceability of national standards,
- the metrology capacity of EURAMET Member States whose metrology programmes are at an early stage of development to be increased,
- organisations other than NMIs and DIs to be involved in the work.

Time-scale

The project should be of up to 3 years duration.