EUROPEAN UNION

Structural Instruments 2014-2020

ELI-NP
Pilot Centre for Medical Applications

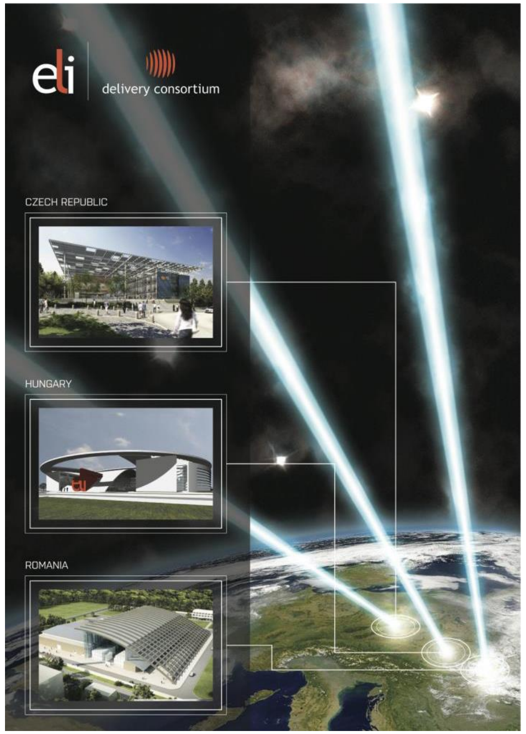
Calin A. UR & Dan STUTMAN – ELI-NP/IFIN-HH

eli nuclear physics

IFIN-HH

ELI-NP – Part of the European Research Area

Extreme Light Infrastructure (ELI)



The largest laser research center worldwide distributed in three countries (RO, HU, CZ)

High-Energy Beam Facility: application of primary and secondary sources of high-energy radiation and particles (*ELI-Beamlines*, Prague, CZ)

Attosecond Laser Science: new regimes of time resolution in broad spectral ranges (*ELI-ALPS*, Szeged, HU)

Nuclear Physics Facility: ultra-intense laser and brilliant gamma beams (up to 19 MeV) enabling novel nuclear and photonuclear studies (***ELI-NP***, Magurele, RO)

Our mission

- To **produce science at the forefront of knowledge** and **generate innovation** with important benefits for society;
- To **attract best users** from the international research community and engender a range of **excellent scientific results**;
- To act as a **hotspot for science, innovation and development**; to develop partnerships with pan-European academic, industrial and entrepreneurial communities and act as a scientific, technological, regional and international hub;
- To **inspire younger generations** and stimulate education and development.

Gerard Mourou
(France)

Nobel Prize in Physics 2018 together with Donna Strickland (Canada)

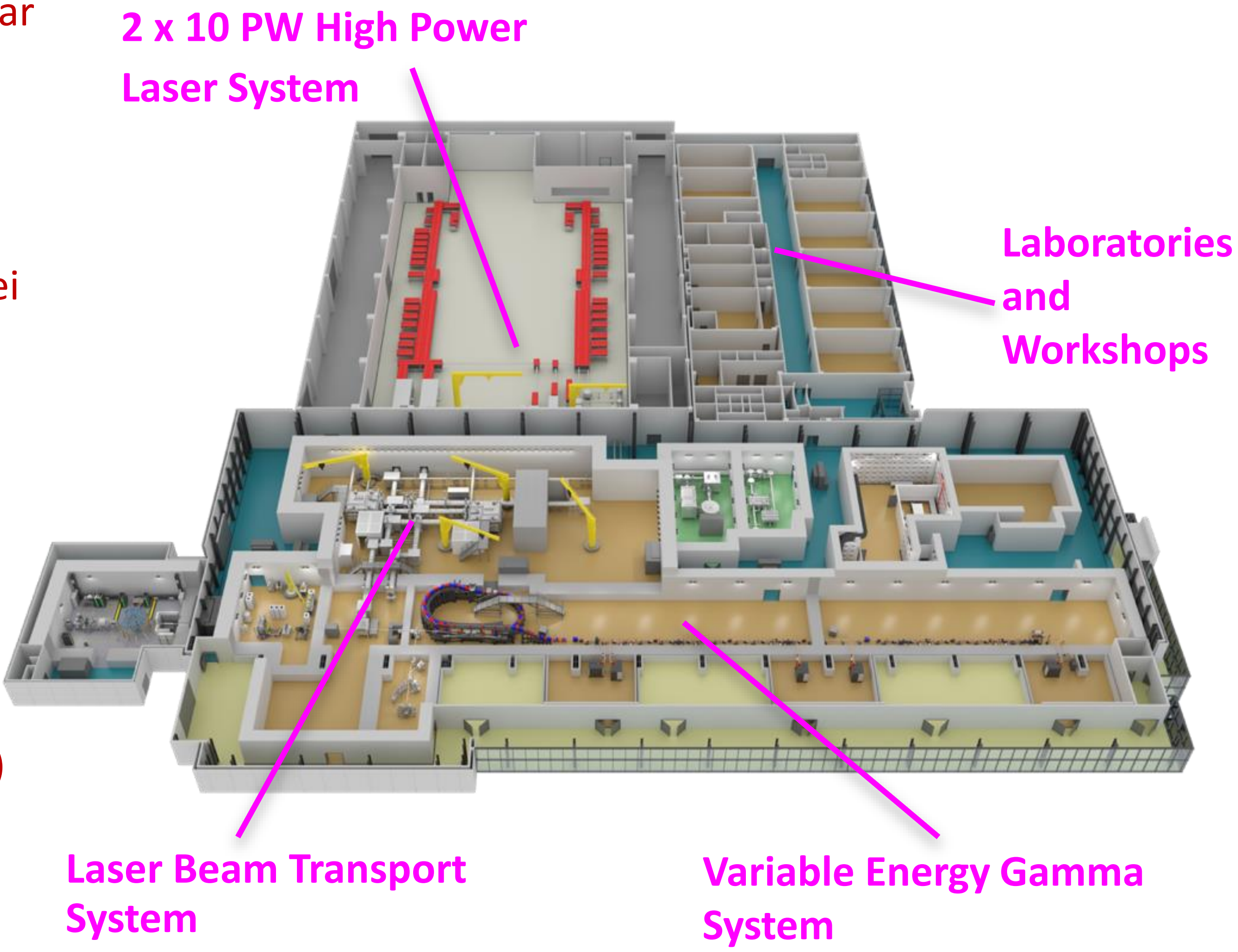
ELI-NP – Physics Case

Advanced studies in basic science ...

- characterization of laser-matter interaction with nuclear methods
- particle acceleration with high power lasers
- nuclear reactions in plasma
- photonuclear reactions, nuclear structure, exotic nuclei
- nuclear astrophysics and nucleosynthesis
- quantum electrodynamics

... and applications – developing technologies for:

- medical applications (X-ray imaging, hadron therapy, radioisotopes generation)
- industrial applications (non-destructive studies with γ)
- material studies with positrons
- materials in high radiation fields

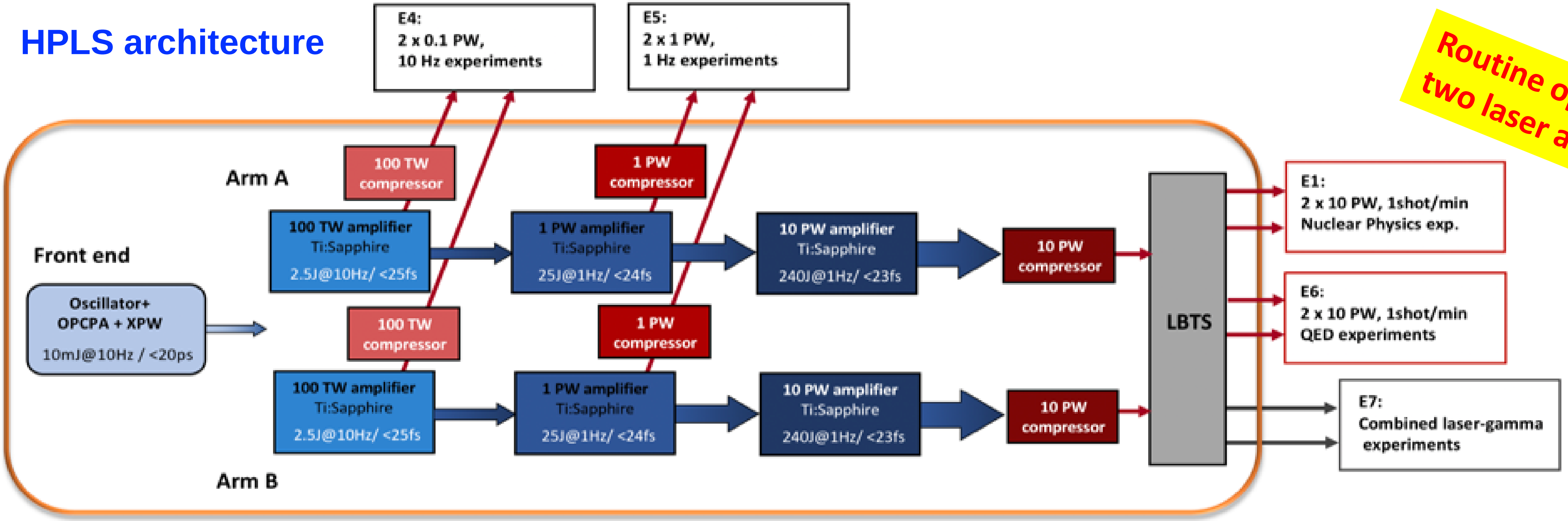


The 2 x 10 PW High-Power Laser System

Measured parameters of HPLS

Output type	100 TW	1 PW	10 PW
Pulse energy (J)	2.5	24	242
Pulse duration (fs)	< 25	< 24	<23
Repetition rate (Hz)	10	1	1/60
Calculated Strehl ratio from measured wavefront	> 0.9	> 0.9	> 0.9
Pointing stability (µrad RMS)	< 3.4	< 1.78	< 1.27
Pulse energy stability (rms)	< 2.6 %	< 1.8 %	< 1.8 %

HPLS architecture



Routine operation with the two laser arms in parallel

The Most Powerful Laser in the World

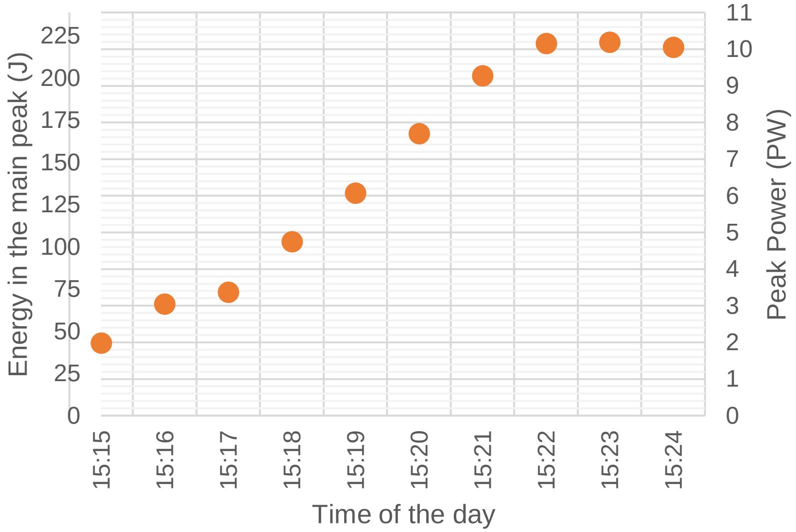
Inaugural 10 PW and User Symposium – Moving into Uncharted Territories

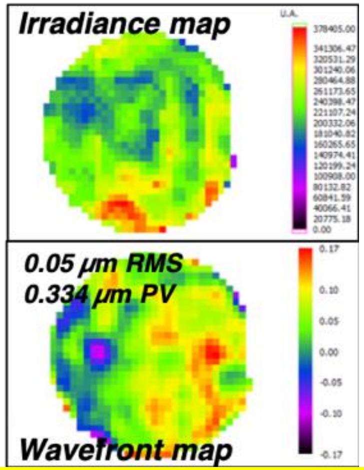
Live demonstration of 10 PW – over 200 participants online – 11.11.2020

<u>Unique system in the world</u>:

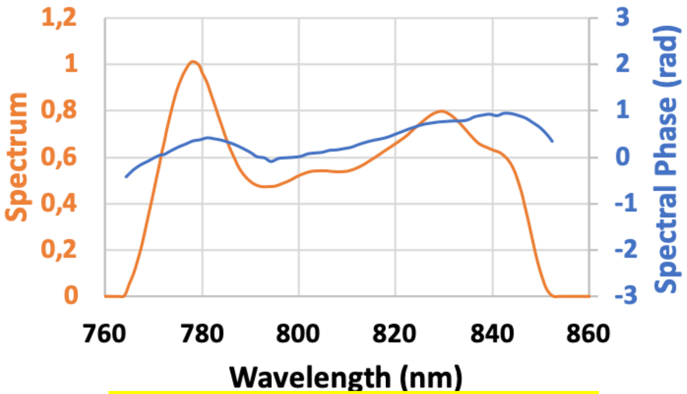
power, intensity, number of beams, versatility and flexibility

- **demonstrated power level 10 PW**
- **combination of 2 high power lasers**

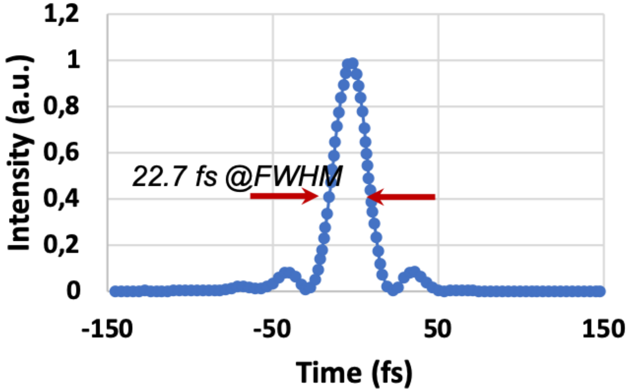




Spatial characteristics



Spectral characteristics

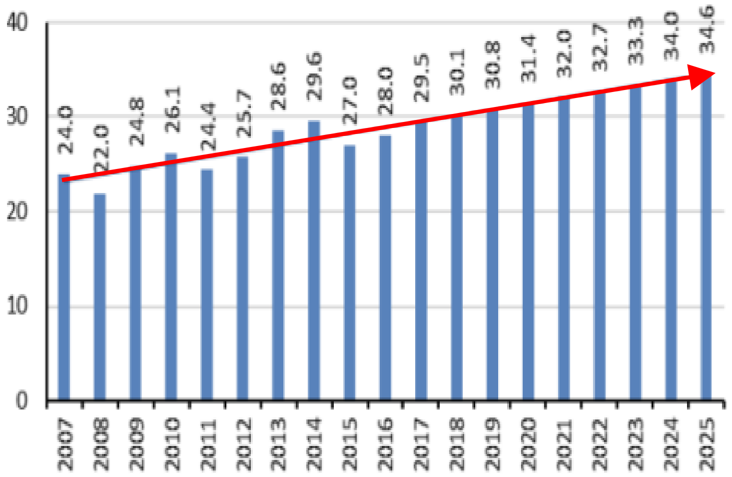


Time characteristics

Research for Medical Applications

- **Societal burden of cancer increasing worldwide and in Romania**
- **Radiotherapy, X-ray imaging, and radioisotopes – essential tools for cancer treatment and detection, but need advances**
  - **Radiotherapy: heavy-ion therapy (e.g. C ions) potentially "gold standard" method, but machines too expensive to be accessible**
  - **X-ray imaging: poor tumor visibility and high radiation dose with existing absorption-based imaging**
  - **Radioisotopes: important for both diagnosis and therapy, but production too costly for less wealthy countries**

Breast cancer incidence in Romania



National Effort to Re-Establish Heavy Ion Cancer Therapy in the United States

Arnold Pompos[1], Robert L. Foote[2], Albert C. Koong[3], Quynh Thu Le[4], Radhe Mohan[5], Harald Paganetti[6] and Hak Choy[1]*

[1] Department of Radiation Oncology, University of Texas (UT) Southwestern Medical Center, Dallas, TX, United States, [2] Department of Radiation Oncology, Mayo Clinic, Rochester, MN, United States, [3] Department of Radiation Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, United States, [4] Department of Radiation Oncology, Stanford University School of Medicine, Stanford, CA, United States, [5] Department of Radiation Physics, University of Texas MD Anderson Cancer Center, Houston, TX, United States, [6] Department of Radiation Oncology, Harvard Medical School and Massachusetts General Hospital, Boston, MA, United States

In this review, we attempt to make a case for the establishment of a limited number of heavy ion cancer research and treatment facilities in the United States. Based on the basic physics and biology research, conducted largely in Japan and Germany, and early phase clinical trials involving a relatively small number of patients, we believe that heavy ions have a considerably greater potential to enhance the therapeutic ratio for many cancer types compared to conventional X-ray and proton radiotherapy. Moreover, with ongoing technological developments and with research in physical, biological, immunological, and clinical aspects, it is quite plausible that cost effectiveness of radiotherapy with heavier ions can be substantially improved.

Lack of radio-pharmaceuticals in Romania

Context național

- Ne confruntăm cu:
  - un acces redus de radiofamaceutice
    - mai puține tipuri decât se utilizează la nivel internațional
    - cantități insuficente și costuri mari de achiziție
  - un număr redus de unități medicale de medicină nucleară
  - liste de așteptare peste limita optimă pentru diagnostic și tratament
  - un număr mare de pacienți care se tratează în afară
  - o capacitate scăzută pentru pregătirea specialiștilor
  - o cercetare sporadică, neintegrată într-un program coerent, aliniată la tendințele internaționale
- In Romania , in fiecare an se efectueaza un numar de 35-40.000 de proceduri utilizând radiofarmaceutice, față de necesarul estimat de10 ori mai mare

High Power Lasers can Make the Difference

- **High power lasers (TW to PW-class) have potential to change all this:**

  - more affordable heavy ion therapy using laser-driven acceleration

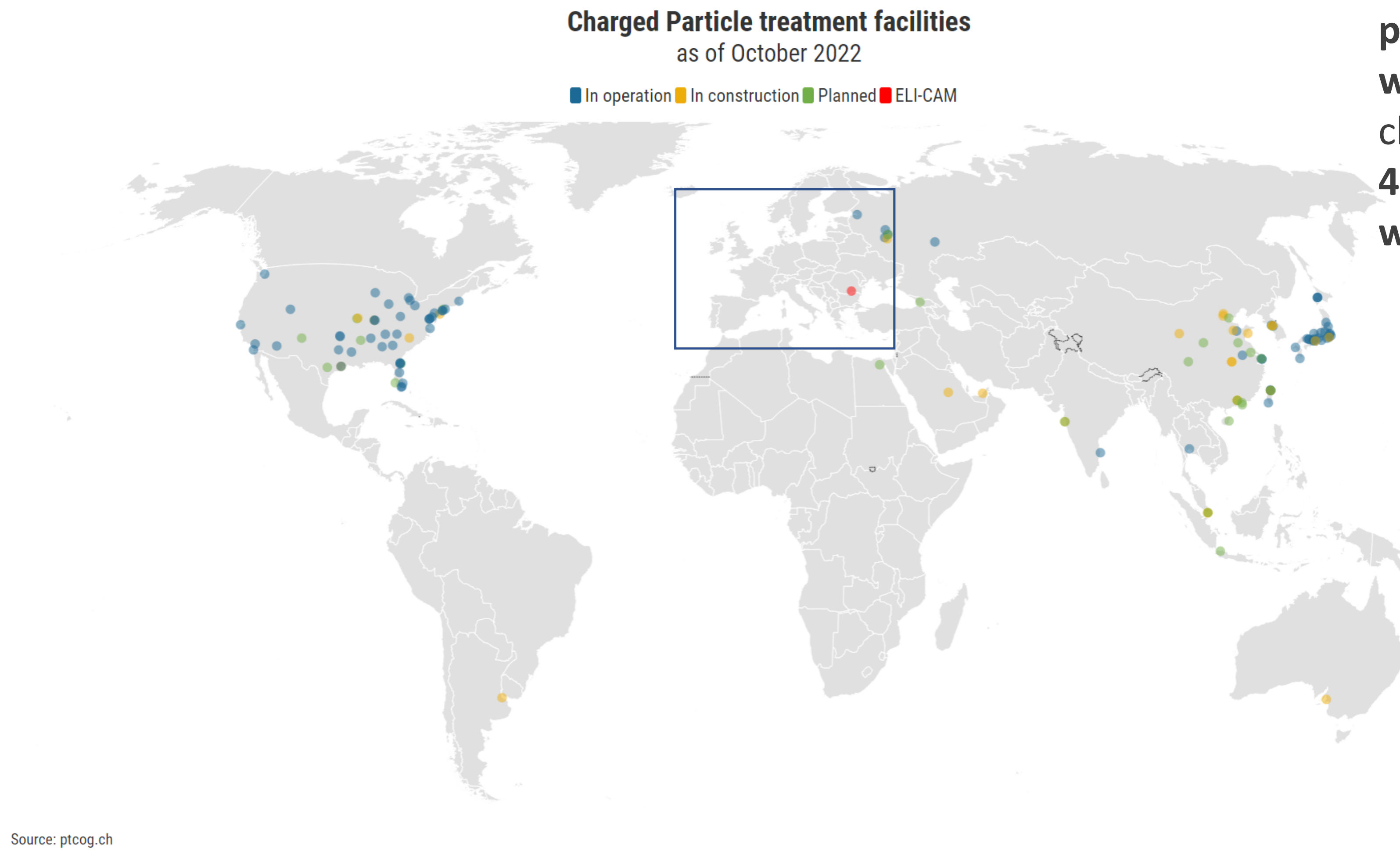
  - improved tumor detection using phase-contrast imaging with laser-driven X-ray source

  - more affordable, local production of radioisotopes using laser-driven nuclear particles/gamma rays

- **ELI-CAM project – in Magurele: construction and operation of a pilot research center for the study, development, preclinical - and later clinical - testing of medical applications of high power lasers**
  - **Main research areas:**
    - **laser heavy-ion therapy**
    - **laser phase-contrast X-ray imaging**
    - **laser medical radioisotope generation**

- **Solutions to be integrated in innovative unitary concept for the treatment and diagnosis of cancer by modern methods**

Hadron Therapy Center Around the World



At end of 2021, about **325,000 patients have been treated worldwide** with Particle Therapy, close to **280,000 with protons**, about **42,000 with C-ions** and **about 3,500 with He, pions and with other ions**.

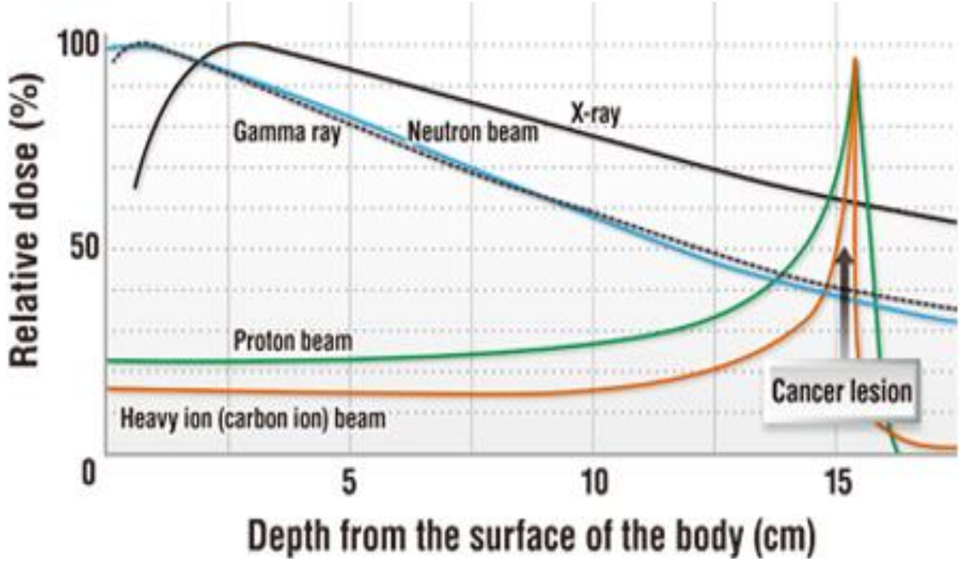
Source: ptcog.ch

Hadron Therapy

Advantages of laser-driven protons or C-ions

- **Heavy-ion (hadrons) irradiation – most precise and localized dose delivery method and highest cancer killing power**
- **Current heavy-ion treatment facilities are huge and extremely expensive (100+ M€), because production, transport and delivery to the patient of high energy, high dose heavy-ions is very difficult when using conventional particle accelerators**
- **10 PW-class lasers have potential to accelerate heavy-ions to therapeutic energy and dose, at ultrahigh dose rate, in few mm**
- **Heavy-ion production can become more affordable and accessible, as laser industry knows to reduce costs (diode pumping)**
- **In addition, laser-driven ultrahigh dose rate heavy-ion irradiation may turn to be the "gold standard" therapy, because it may combine above benefits with the FLASH effect (healthy tissue sparring); conventional accelerators cannot do this**
- **Proposed medical focus: start from skin-level cancer, progressing to breast cancer (#1 cause of cancer mortality for women)**

Bragg peak



Bragg peak. This phenomenon is exploited in particle therapy of cancer, specifically in proton therapy, to concentrate the effect of light ion beams on the tumor being treated while minimizing the effect on the surrounding healthy tissue.

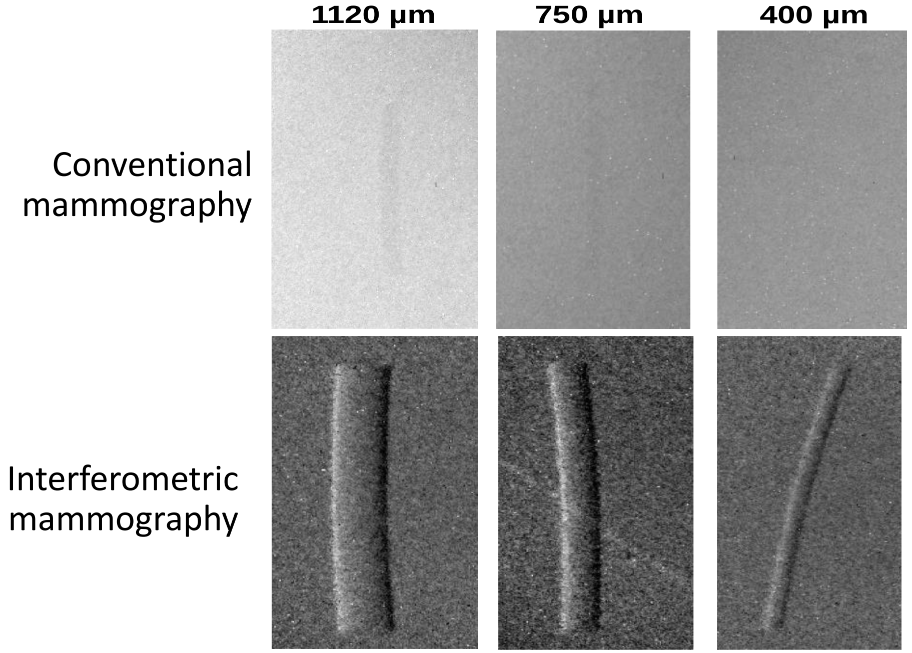
Interferometric Phase Contrast X-ray Imaging

- **Poor visibility of soft tissue tumors and elevated patient radiation dose in conventional, absorption-contrast X-ray imaging**
- **Breast cancer screening by mammography: 20% missed cases, 50% 10-year false positives, not possible under age 40 (dense breasts)**
- **Lung cancer screening by plain chest radiography not possible**
- **Image guidance/treatment planning in hadron therapy not accurate enough (better precision of hadron beam than of imaging)**
- **Phase-contrast X-ray imaging investigated worldwide as alternative**
- **Proposed medical focus: breast cancer, and later lung cancer**

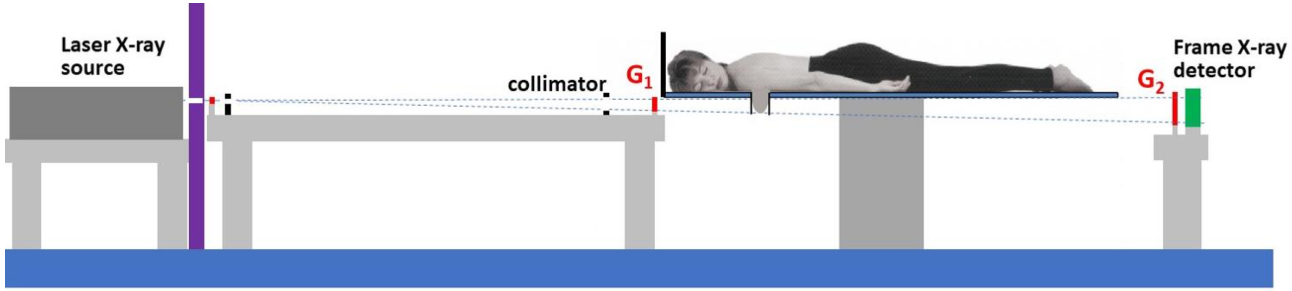
Breakthrough phase-contrast imaging method at ELI-NP using ultrahigh sensitivity, multi-meter long X-ray interferometers

Method requires intense, directional, short-pulse and spatially coherent (µ-focus) X-ray source; **100 TW class lasers can do this!**

Fibrils simulating early breast cancer in mammographic accreditation phantom



Laser-based interferometric X-ray imaging for more sensitive and precise cancer detection and hadron therapy image guidance/treatment planning



Ultrahigh sensitivity X-ray interferometry at ELI-NP (N Safca et al, Phys Med Bio 2022)

Laser-Driven Radioisotopes Production

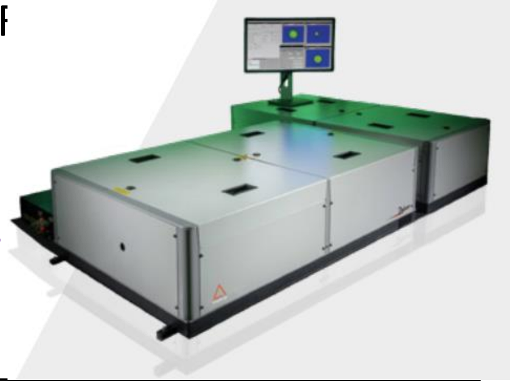
- **Radioisotopes have a central role in nuclear medicine,** being intensively used for the diagnosis and treatment of cancer
- In order not to expose the body to high doses of radiation, **most medical isotopes must have relatively short lifetimes,** which would require ideally radioisotope production to be located "on-site" near the clinics and hospitals where they are used
- **Conventional accelerators (cyclotrons) are currently** used to this end but costly, big, and need extensive radiation protection
- **High power lasers offer an advantageous alternative for producing medical radioisotopes** due to their ability to accelerate different types of particles and generate different nuclear reactions by simply changing the type of target in front of the laser beam
- **In addition, the "*on-site*" production of medically important short-lived radioisotopes, such as ^{15}O, is difficult with conventional cyclotron accelerators, but becomes feasible with lasers**
- **100 TW-class high repetition rate laser sufficient for radioisotope production**

What about the local situation?

In Europe, there is a **discrepancy between western countries and the rest**, the access of patients to modern techniques is far from being equal.

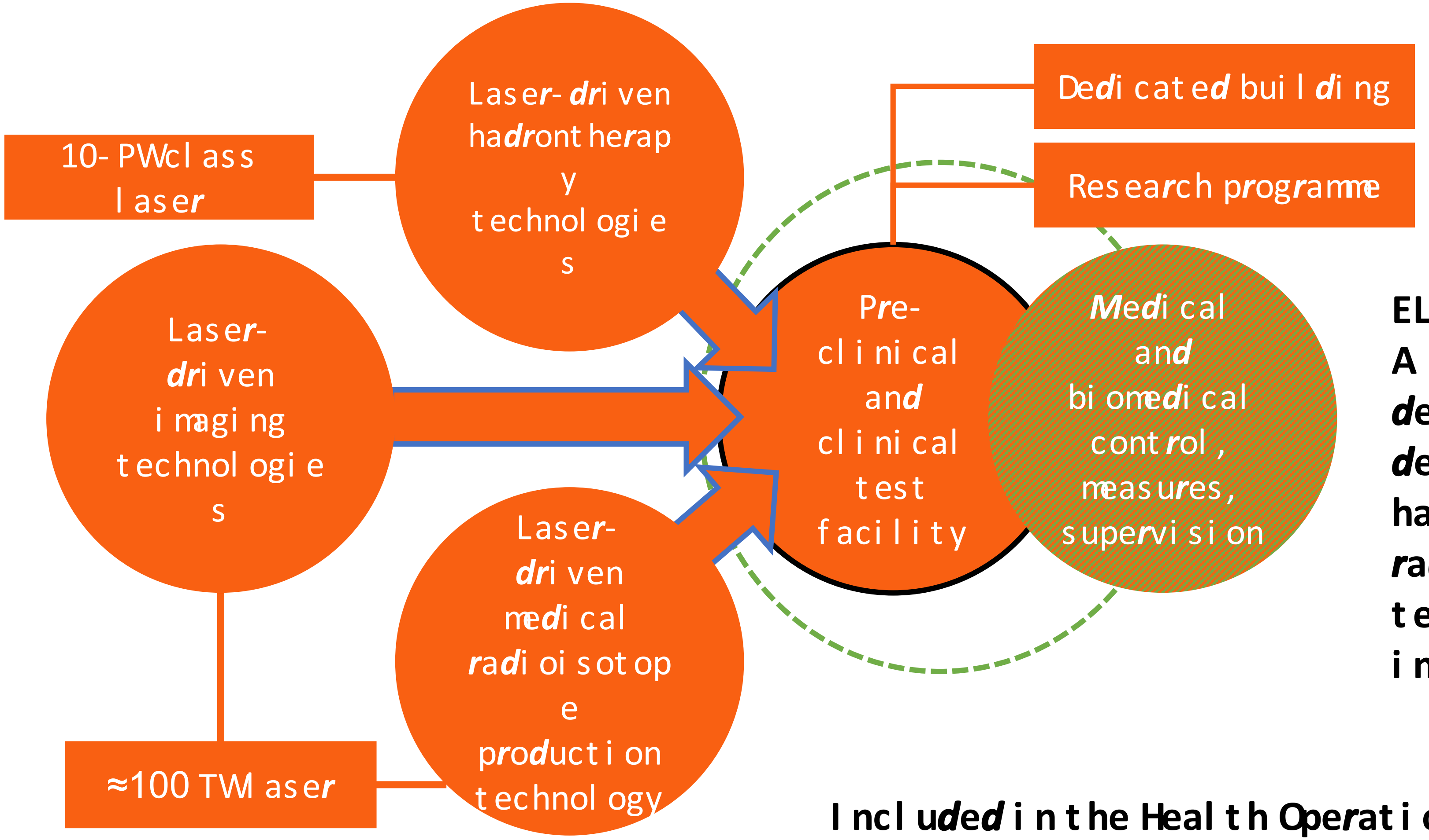
In Romania, with about 20 million citizens, the number of PET scans is less than 10,000/annually, and SPECT procedures about 3 times higher; while about only one person in 2,000 uses diagnostic nuclear medicine each year (vs. 1 person in 50 in western Europe) and these include investigations made in non-EU countries (i.e. Turkey).

In the sub-region (Balkans, Eastern Europe), the situation is similar to R



100 TW-class laser

The Concept of ELI-CAM



ELI-CAM:
A 3-in-1 medical application development facility designed to take laser-driven hadrontherapy, imaging and radioisotope production technologies closer to industrial maturity

Included in the Health Operation Program 2022 – 2029
Priority 5: research

The Concept of ELI-CAM

- **10 PW-class laser needed to accelerate heavy-ions to therapeutic energies**
  - **ELI-NP only facility in the world with operational 10 PW lasers**
- **Phase I: Basic/foundational research stage using the ELI-NP lasers is necessary:**

  - find and optimize best acceleration scheme for therapeutic heavy ions

  - develop ion transport, dosimetry, irradiation, radiobiology systems

  - perform preparatory in-vitro and in-vivo irradiation studies
- **Phase II: ELI-CAM Center proposed as a distinct infrastructure from ELI-NP, housed in its own building, with its own high power lasers, and a distinct R&D and operation team**
  - This approach needed because research, innovation, development and testing of medical applications are **highly intensive specialized activities**, requiring permanent access to lasers and fixed experimental arrangements; Because **ELI-NP is a user-facility**, access time to high power lasers will be increasingly limited and experimental arrangements frequently modified
- **The Center will include radiation and imaging rooms for preclinical and later clinical testing, as well as telemedicine capabilities to enable collaboration and remote working of medical partners and collaborators**