APPLICATIONS OF HIGH-POWER ULTRAFAST LASERS DRIVEN X-RAY SOURCES

Jean Claude Kieffer
INRS-EMT
1650 blvd L. Boulet, Varennes, Qc, Canada

ALLS
Advanced Laser Light Source

Key collaborators

Jean-Luc Bourgade (CEA)
Sylvain Fourmaux (INRS)
Emil Hallin (GIFS)
Andrzej Krol (SUNY)
Victor Malka (Weizmann)
Gérard Mourou (Polytechnique)

PART I: FROM LIGHT TO IMAGE:

illustration through early breast cancer detection and global food security challenges

- Introduction
- Breast Cancer
- Global Food Security
- Conventional imaging Technique
- Ultrafast Laser-based X-ray sources
- Imaging & X-ray holography

Introduction

THE GENERAL GOAL

Correlating macroscopic expression to interaction with environment

A COMMON CHALLENGE FOR DIFFERENT FIELDS

THE STRATEGY (ACTION PLAN)

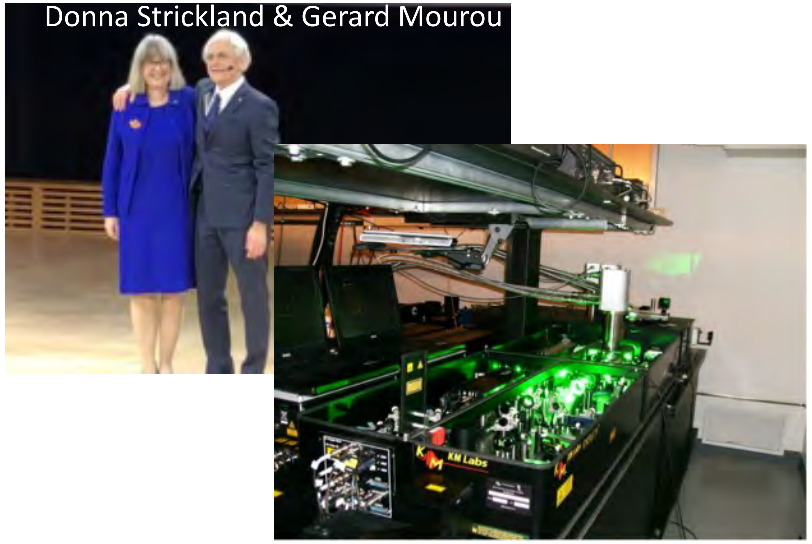
Doing a machine based on high power Laser-matter interaction

Bringing the machine inside the User world (Hospital, Farm)

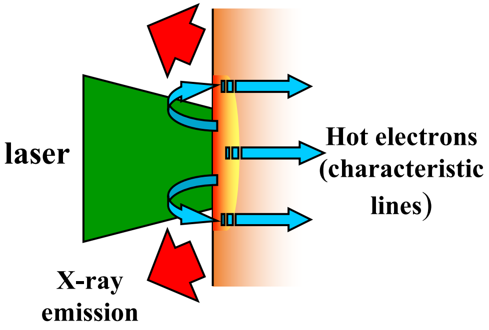
THE TACTICAL APPROACH (EXECUTION PLAN)

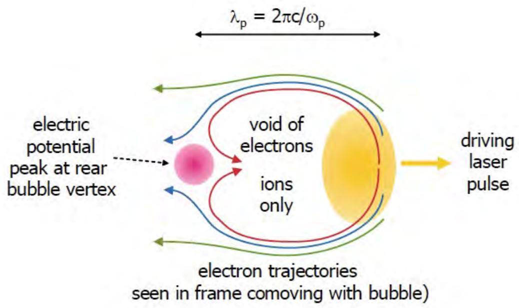
Integrating blocs and technologies

Ultrafast laser



Laser-based X-rays

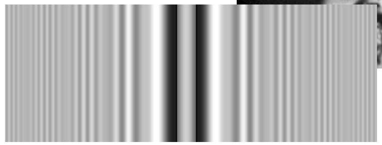




X-ray holography

1816
Augustin Fresnel

1933
Frederic Zernike



THE TACTICAL APPROACH (EXECUTION PLAN)

Multidisciplinary programs: a very complex reality

Breast Cancer

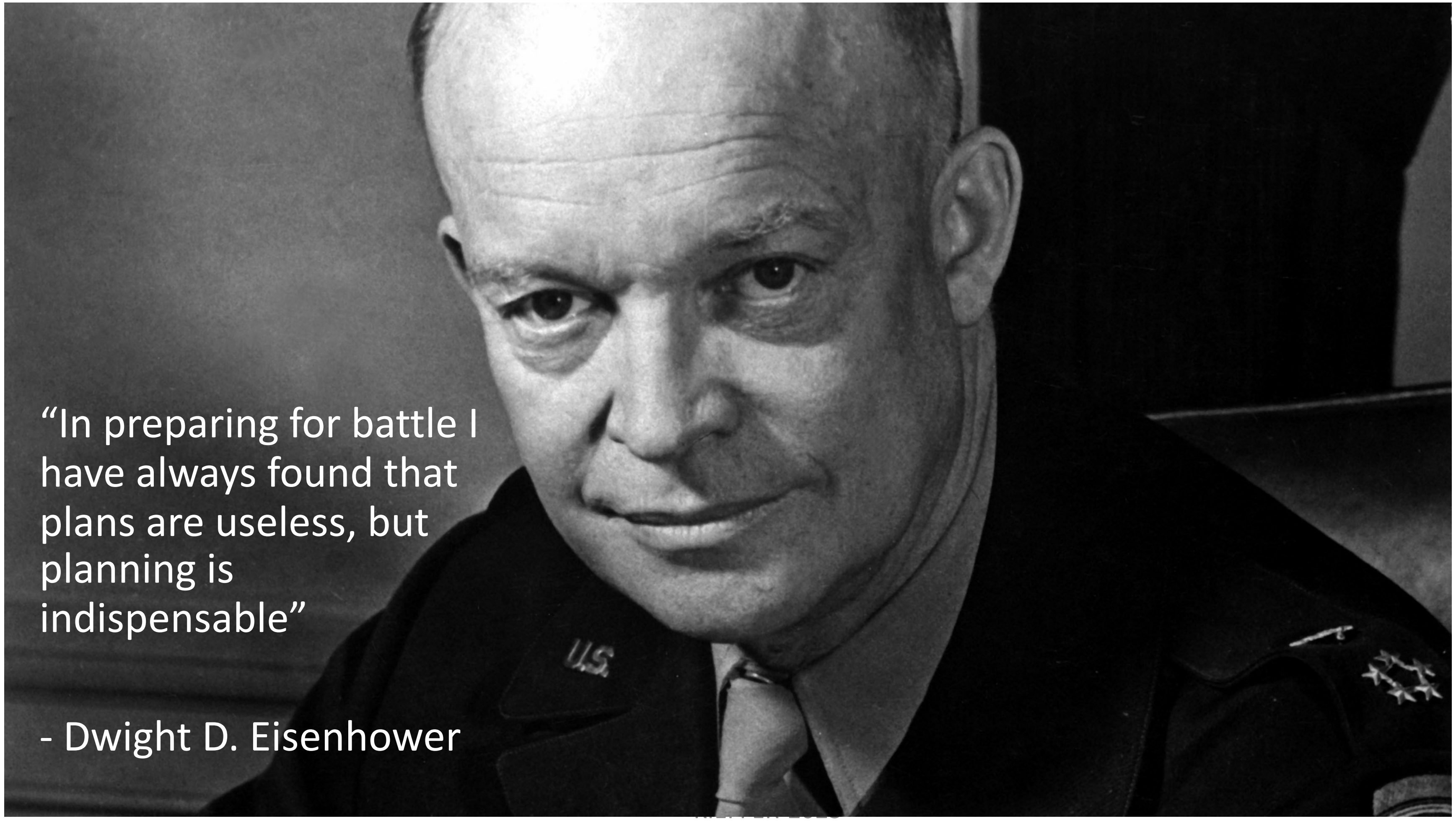
- *The Upstate Medical U (SUNY - Syracuse) Dept of Radiology and Radiation Therapy*
- *The Hospital « Sacré-Cœur » & « Notre Dame » Dept of Radiology & Medical imaging (Montreal)*
- *The Hospital « La Timone » Small animal imaging (Marseille)*
- *The U of Michigan (CUOS - USA)*
- *The CSIRO (Australia)*
- *The U of Aix-Marseille (LP3 - France)*
- *Amplitude Technology*
- *INRS (EMT and IAF (Small animal facility))*

Global Food Security

- *The Global Inst. for Food Security (Sask)*
- *The U of Saskatchewan, Dept of Biology (Sask)*
- *The Botanical Garden of Montreal (Montreal)*
- *The U of Guelf (Controlled Environt systems)*
- *The Canadian Light Source inc.*
- *Thales laser*
- *INRS (EMT)*

THE TACTICAL APPROACH (EXECUTION PLAN)

Looks like a good plan



Breast cancer

BREAST CANCER IS THE MOST PROMINENT CANCER

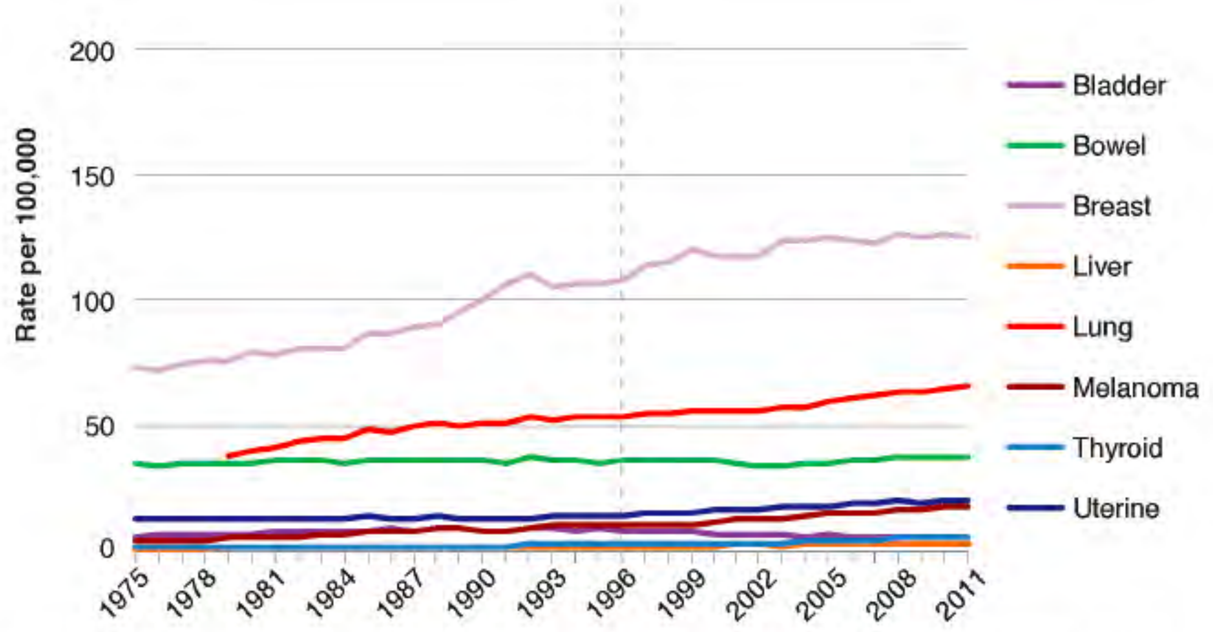
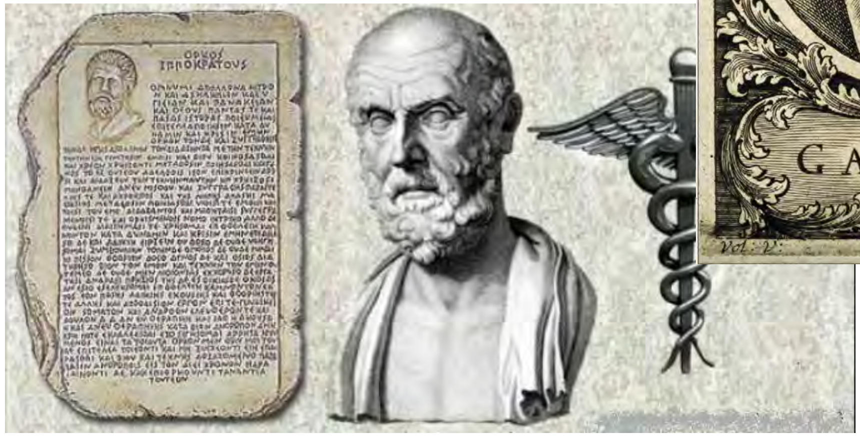


FIGURE 5-6 Cancer incidence in women in the United Kingdom, 1975–2011.
DATA SOURCE: Cancer Research UK. Available at http://www.cancerresearchuk.org/health-professional/cancer-statistics. Accessed October 30, 2015.
NOTE: Dashed line at 1996 indicates year GE soybean and maize were first grown in the United States.

BREAST CANCER IS THE MOST PROMINENT CANCER



Hippocrates (460-370 BC)

Galen (121-223 BC)

VALUE IN HEALTH | JANUARY 2022

POSC129

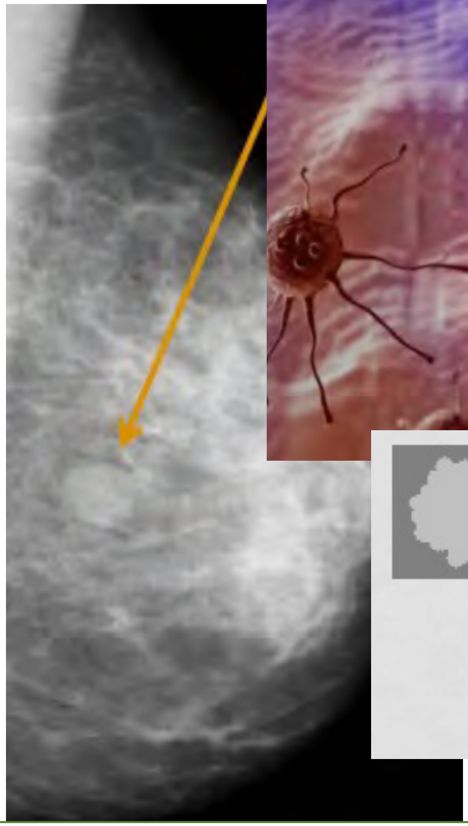
ECONOMIC BURDEN OF METASTATIC BREAST CANCER IN GREECE

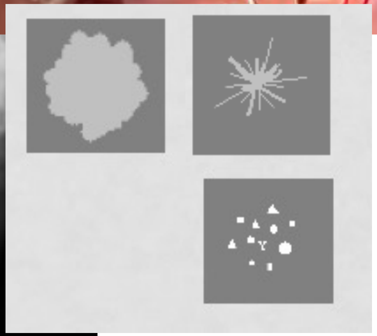
Stafylas P,[1] Avgitidou A,[1] Karaiskou M,[1] Nikolaidis D,[2] Tigka A,[2] Stathelou L,[2] Kesisis G,[3] Boukovinas I[4]

[1]HealThink, Thessaloniki, Greece, [2]Novartis Hellas Pharmaceutical Company, Athens, Greece, [3]Agios Loukas Clinic, Thessaloniki, Greece, [4]Bioclinic Oncology Unit of Thessaloniki, Thessaloniki, Greece

Objectives: Breast cancer (BC) is the most commonly diagnosed cancer in women and the second leading cause of cancer death in Greece. The economic burden of BC is substantial and has been steadily increasing. The aim of this study was to provide the first estimate on the direct costs associated with the management of metastatic BC (mBC) in Greece. ***Methods:*** The methodology used in our study follows the standards of the micro-costing approach in cost-of-illness (COI) analyses. A retrospective COI study was conducted from the Greek National Organization for Health Care Provision perspective for a 12-month period. The prevalence of mBC derives from the data available at GLOBOCAN and recent bibliography. The total number of mBC patients in Greece is estimated at 1.786. The COI model approximates the real-life annual cost of mBC as the sum of drug acquisition, resource use, adverse events management, and hospitalization costs. ***Results:*** The annual cost of mBC in Greece was estimated at €89,949,376. The key cost driver is the drug acquisition cost of disease-specific treatments, which is estimated at €72,176,624 (80.24% of the total cost). Of the total cost, 12.27%, 3.20%, 3.03%, and 1.25% represent the drug acquisition cost of supportive treatment, resource use, hospitalization, and adverse events management costs, respectively. Total costs of managing mBC per patient per year are estimated at €49,974. ***Conclusions:*** The results from the present analysis show that mBC comprises a significant economic burden for the Greek healthcare system, mainly driven by disease-specific treatment costs. Despite some limitations, the present study constitutes the first comprehensive COI analysis in patients with mBC and provides health care decision-makers with an insight into the substantial cost of mBC in Greece. In light of the clinical and economic burden associated with mBC, new therapeutic options, ideally accompanied with biomarkers, are of high value.

ULTIMATE X-RAY RADIOGRAPHY

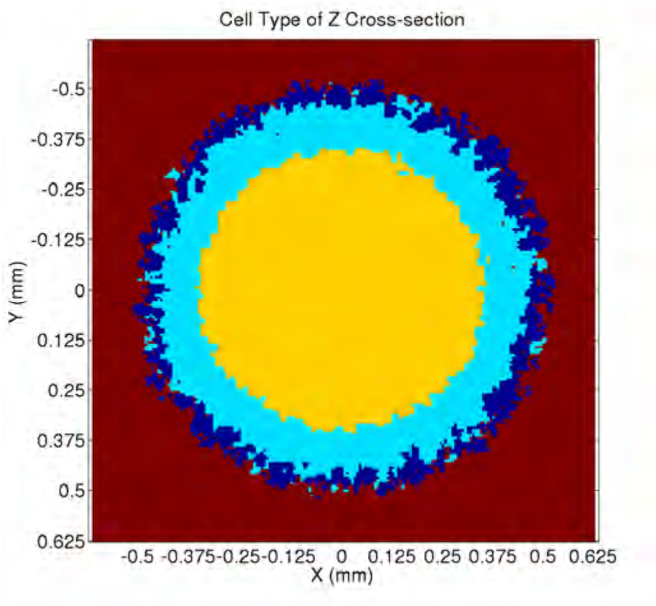




LOWER DOSE FOR PATIENT
IMAGE QUALITY FOR SPECIFICITY
VERY HIGH RESOLUTION FOR EARLY DETECTION
LESS INVASIVE MODALITIES

Visualize early tumor development with penetrating radiation (Prof. A. Krol - SUNY)

NEED TO DETECT INTERACTION AT EARLY STAGE TO UNDERSTAND/CONTROL GROWTH



Seeing tumor vascularization.
Interaction tumor-tissues

- ✓ *Need penetrating radiation*
- ✓ *high contrast*
- ✓ *0.1µm – 10µm resolution*
- ✓ *Spatial frequency*

Global Food security

Food security is a vital concern

IN 2050

TODAY

- *2 billion people go to bed hungry*
- *2 billion people are facing malnutrition and obesity*
  (Les echos, Sept 2018, p48)

Agriculture challenges at the horizon 2050

✓ ***Local level***

- *Facing modifications of our local environments due to climate change*

✓ ***Global level***

- *Feeding a growing world*

Science Breakthroughs to Advance Food and Agricultural Research by 2030

Committee on Science Breakthroughs 2030:
A Strategy for Food and Agricultural Research

A Consensus Study Report of

The National Academies of

SCIENCES · ENGINEERING · MEDICINE

118TH CONGRESS
1ST SESSION

H. R. 1697

To enhance the participation of precision agriculture in the United States, and for other purposes.

IN THE HOUSE OF REPRESENTATIVES

MARCH 22, 2023

Mr. DAVIS of North Carolina (for himself and Mr. MANN) introduced the following bill; which was referred to the Committee on Agriculture

Agriculture challenges at the horizon 2050

Farm size made solution complex

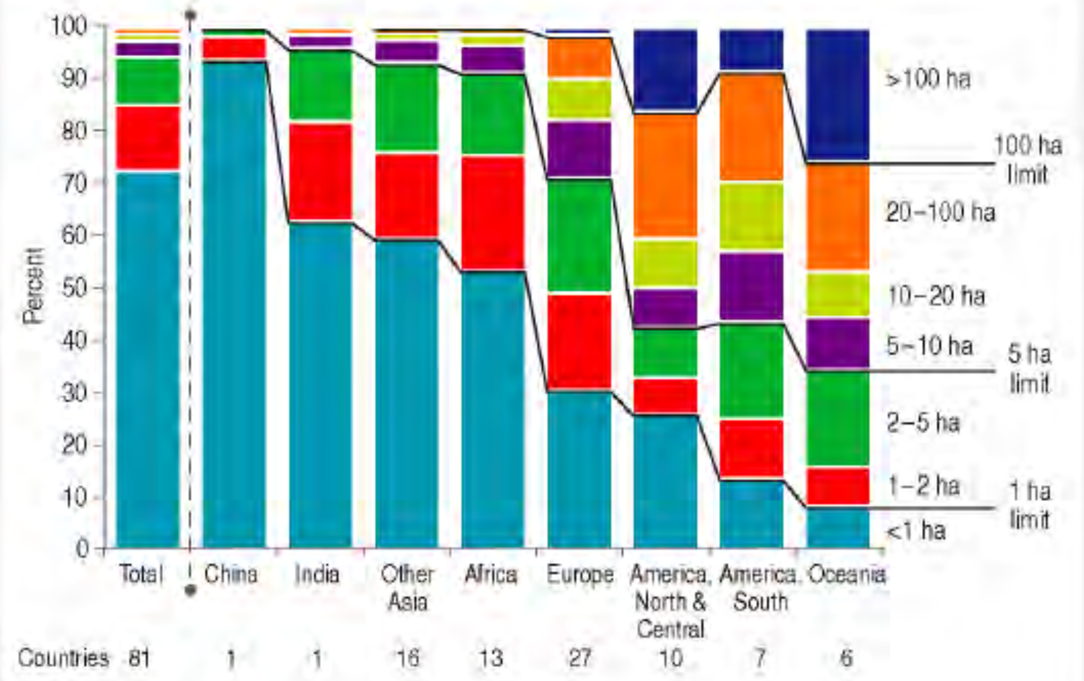


FIGURE 6-1 Diversity in farm size by region.
SOURCE: HLPE (2013).
NOTE: Figure is based on data from 81 countries.

The Greek CAP strategic plan

2. GOALS AND STRATEGY OF THE CAP STRATEGIC PLAN OF GREECE

The Greek CAP Plan responds to modern challenges through a balanced approach to the ambitions of the new CAP for a more resilient, green and digital agriculture, in line with the priorities of the European Green Deal. It marks the shift towards a new production model for Greek agriculture and

In Greece. The Plan focuses on improving competitiveness by promoting

logies, fostering young entrepreneurship and securing a fair income for

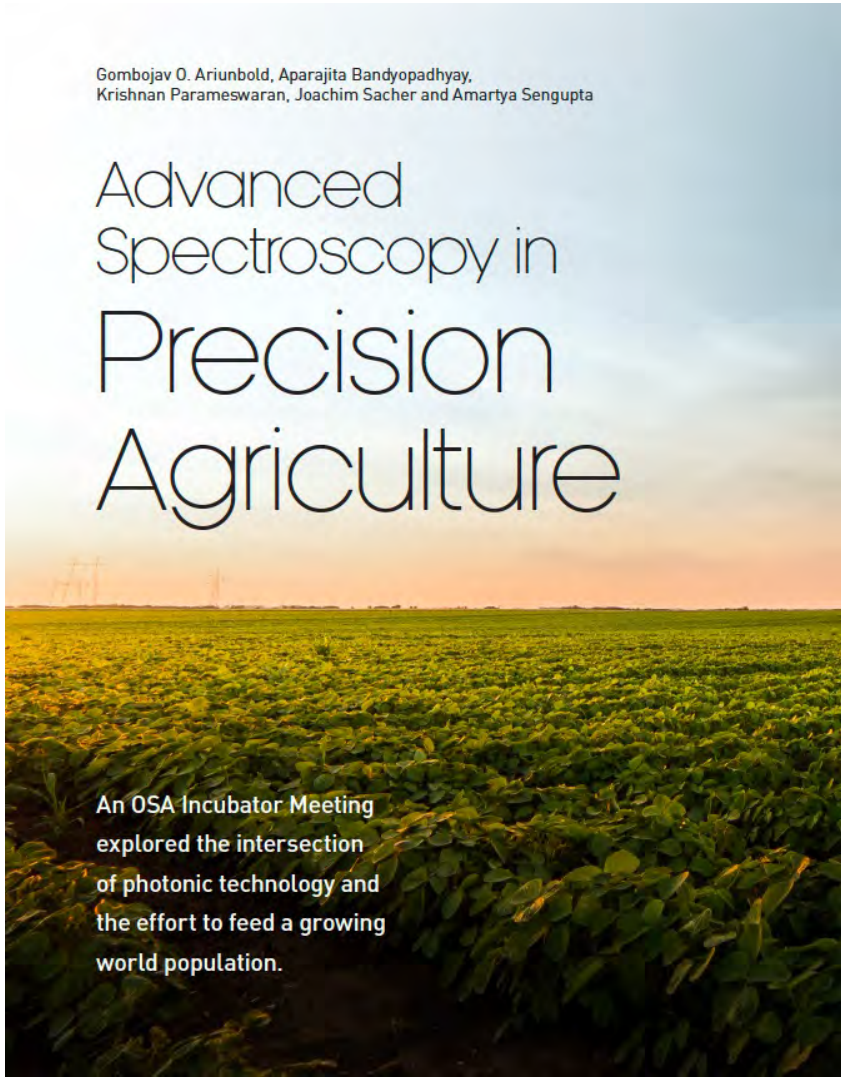
n aims to reduce the environmental footprint of agriculture. The main

able development of rural areas.

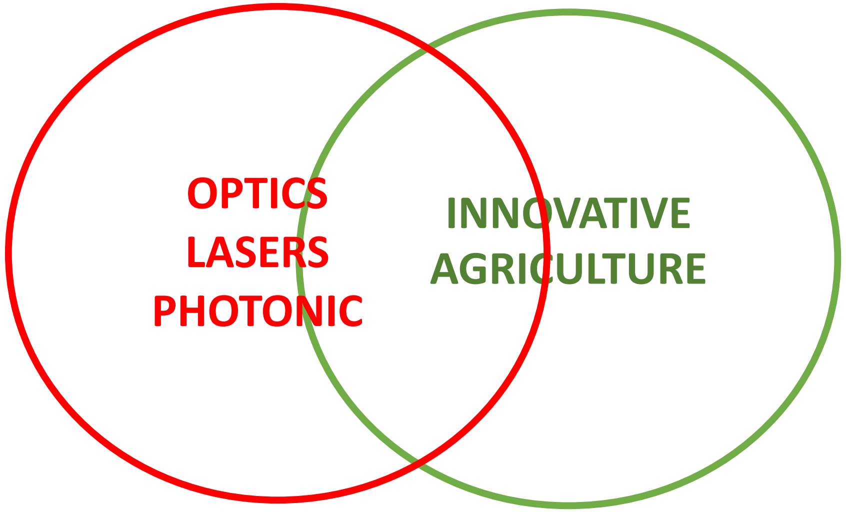
The **Greek agricultural sector employs approximately 400 000 people**, representing 10% of employment in all sectors. The farm labour force consists mainly of family holdings. Unemployment in rural areas remains an issue, especially for young people, in light of the aging population. More than 70% of the Greek agricultural area faces natural or other specific constraints (for example: extreme slopes, low temperatures, dryness of soil, unfavourable soil texture, borderline areas, island regions) which significantly affect farming.

- **Rural areas represent 63% of the Greek territory** and the agricultural land amounts to approximately 5.3 million hectares.
- **Rural inhabitants represent 31% of the Greek population**, a share higher than the EU average.
- **Greek agriculture consists of about 700 000 farms**, which are rather small in **physical size with the average farm being 7 hectares**. In fact, more than 70% of the farms consist of less than 5 hectares.

Agriculture challenges at the horizon 2050



Understanding and monitoring plant physiological processes is key to respond to the challenge of feeding 10 billion people in 2050

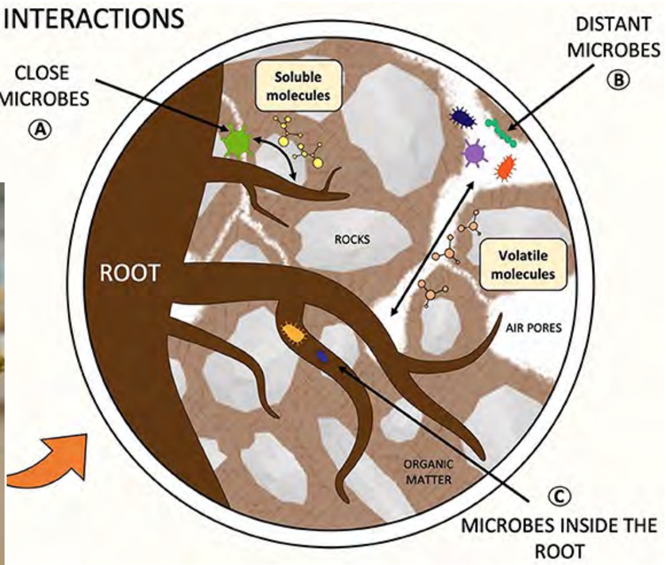


Global food security: A Canadian initiative (2015)

correlating phenotypic expression with adaptation to environmental stress

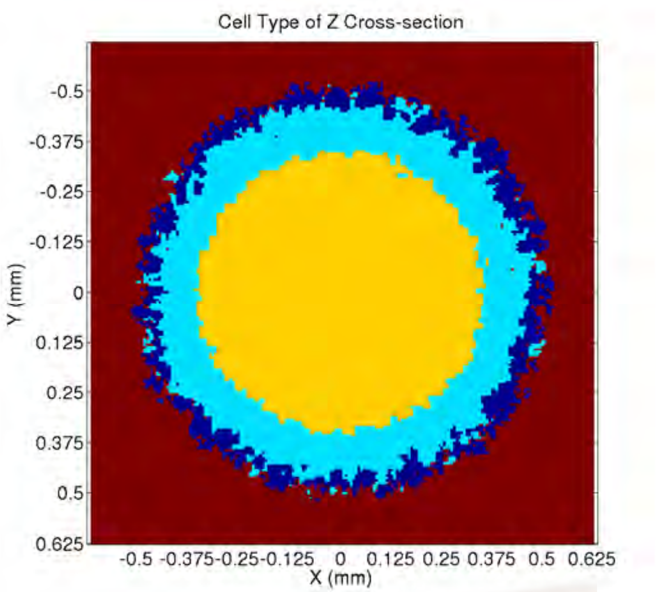
Visualize intact rhizospheres with penetrating radiation (Dr E. Hallin - GIFS)

ULTIMATE X-RAY RADIOGRAPHY



Ariotti Cet al, (2020) The Fascinating World of Belowground Communication. Front. Young Minds. 8:547590. doi: 10.3389/frym.2020.547590

NEED TO DETECT INTERACTION AT EARLY STAGE TO UNDERSTAND/CONTROL GROWTH



Seeing tumor vascularization. Interaction tumor-tissues

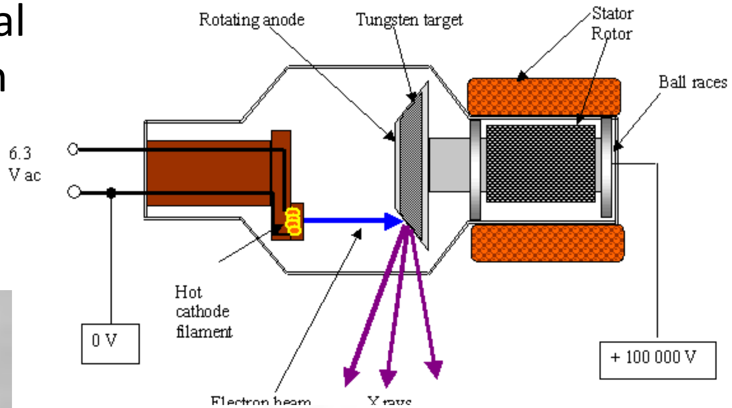
- ✓ Need penetrating radiation
- ✓ high contrast
- ✓ 0.1µm – 10µm resolution
- ✓ Spatial frequency

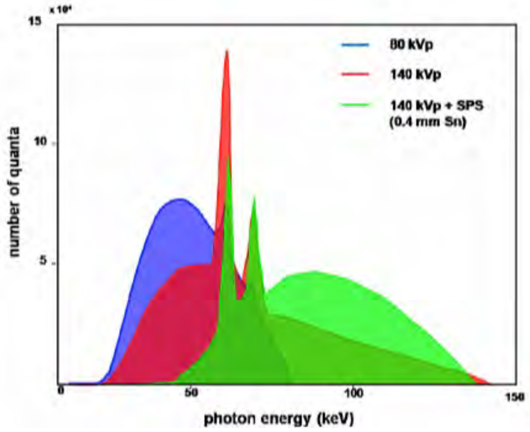
Seeing interaction roots-soil

CONVENTIONAL IMAGING TECHNOLOGY

Screen-film mammography

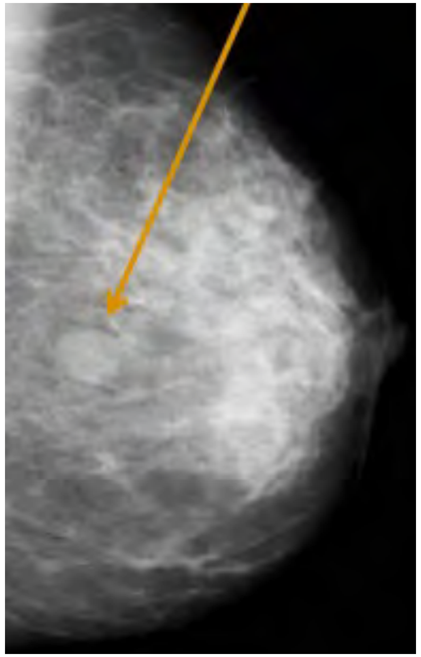
The clinical and preclinical X-ray imaging is based on conventional X-ray tube technology initiated in 1895.





Conventional machines widely used for mammography
But still limited performance

Detection at the 1/2mm size
Painful procedure



- 460,000 breast cancer deaths have been averted in US women from 1989 to 2020.
- Declines in breast cancer mortality have been attributed primarily to early detection through screening mammography.
- However, current state-of-art screening mammography is underperforming for dense breasts due to mismatch of x-ray energy vs. breast density.
- Further, it would be desirable to lower the radiation dose and improve specificity and sensitivity of mammography for all types of breast tissue.

DOSE IS A CONCERN

- **0.04mSv:** 1 Flight Montreal – Paris (6µSv/h)

- **1mGy/Y/person** (1mSv/Y/person):
  limit allowed for population

- **1 - 3mGy/mammography** (for a 40mm thick breast): dose for one mammography (glandular mean dose)

- **2Gy**: Cancer radiotherapy treatment

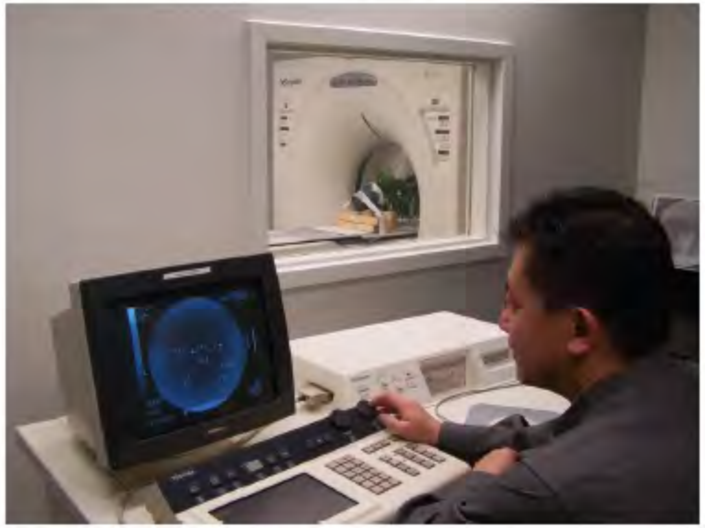
  - **5Gy** (5Sv): fatal dose

  - **100Gy**: at Hiroshima Hypocenter

The patient confort is also a concern

Conventional machines widely used for plants and trees Imaging but not adapted

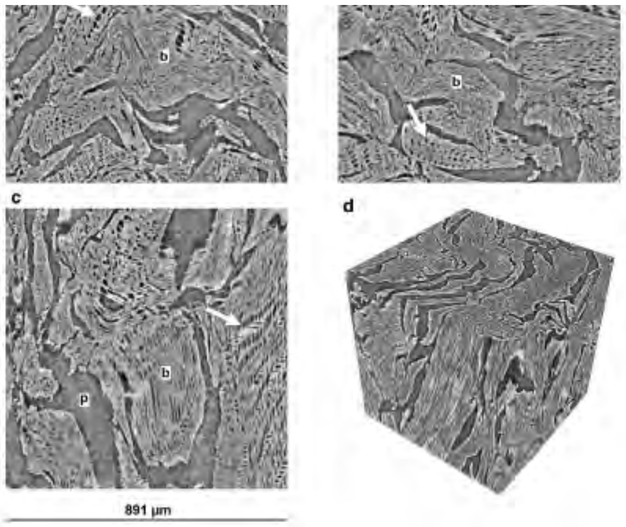
Fig. 4. View of a computed tomography (CT) scanning session at the CT Scanning Laboratory for Agricultural and Environmental Research on Macdonald Campus of McGill University, for a pyramidal cedar (*Thuja occidentalis* 'Fastigiata') (Dutilleul et al. 2008). [Colour online.]



676 Biochar (2021) 3:671–686

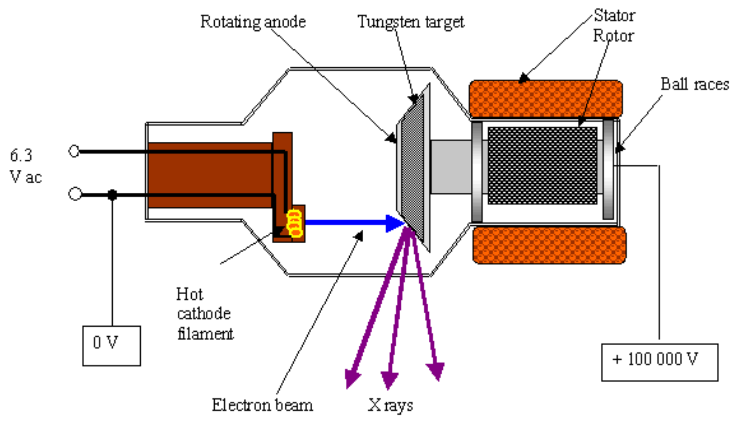
Fig. 1 Illustrations of the SWP550 biochar structure, as reconstructed from X-ray microtomography data. Presented are orthogonal cross sections (**a** *X–Y*-plane; **b** *Y–Z*-plane; **c** *X–Z*-plane) and a 3D rendering (**d**) of the cropped image cube. The small letters "p" and "b" indicate pore spaces and biochar structures, respectively. Arrows point to areas that had a stronger resemblance to the cellular structures found in softwood

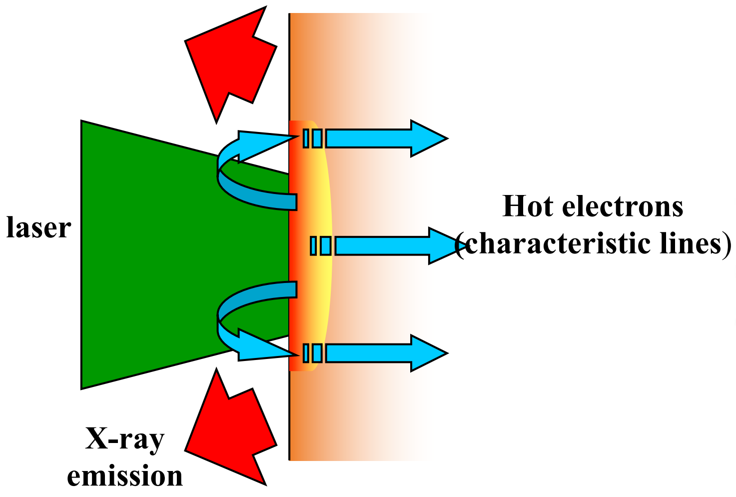
Big machine
Lack of resolution to see rizhospheres

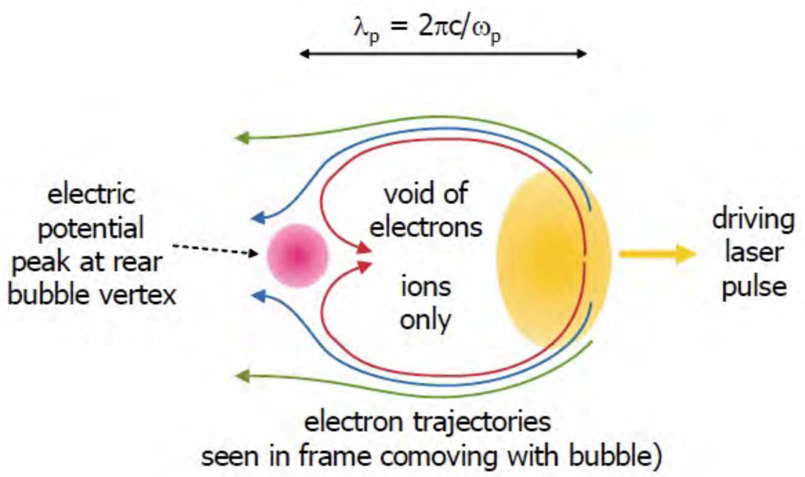


ULTRAFAST LASER-BASED X-RAY SOURCES

Is there a future for a laser-based X-rays?







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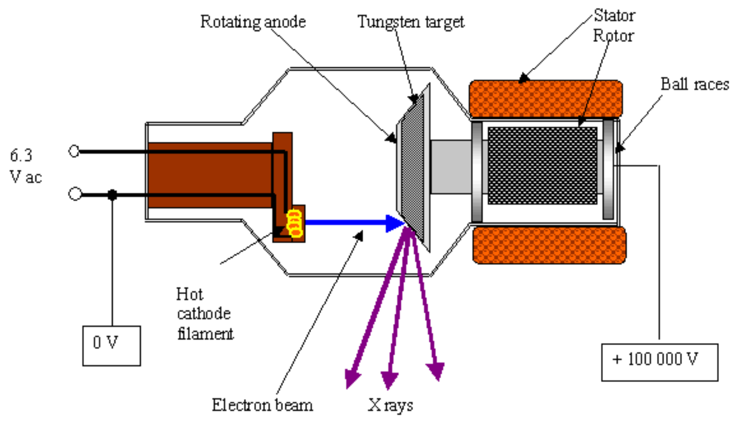

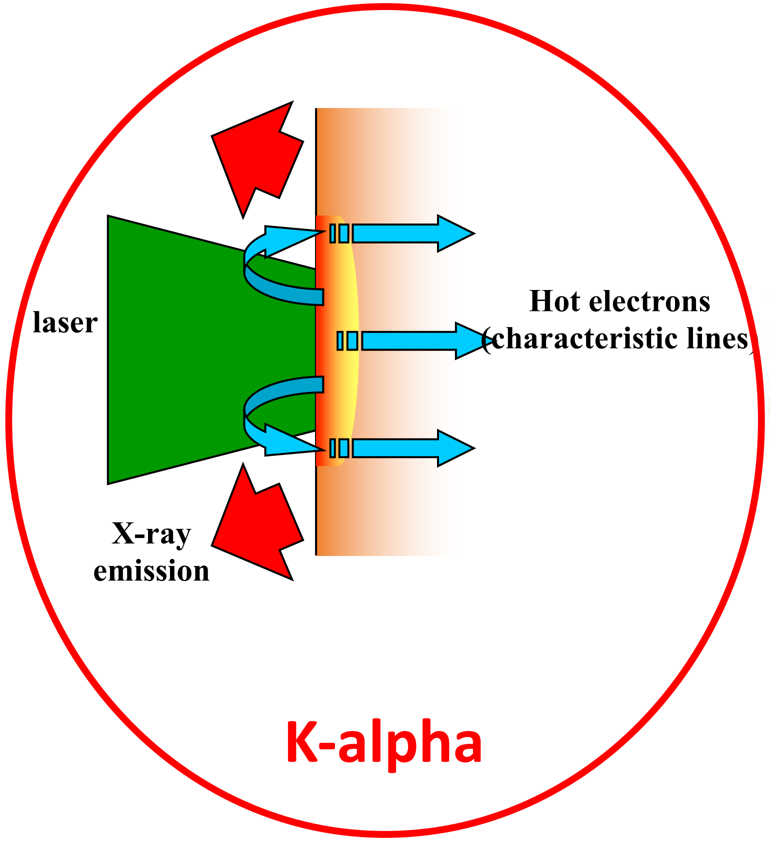

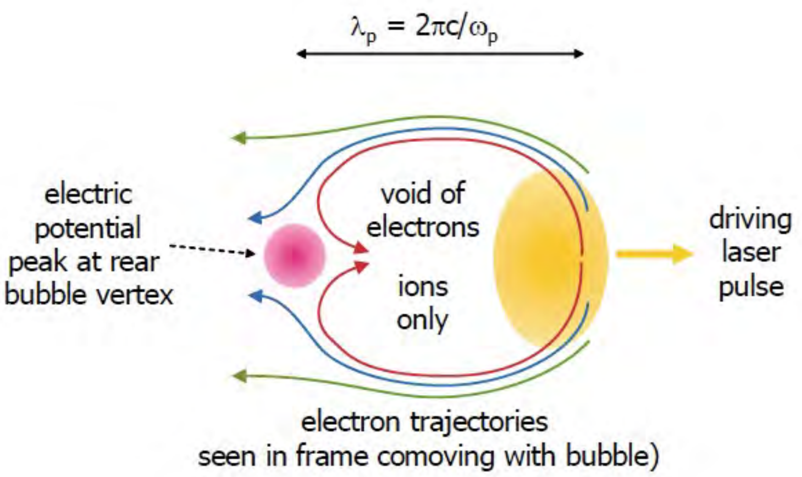

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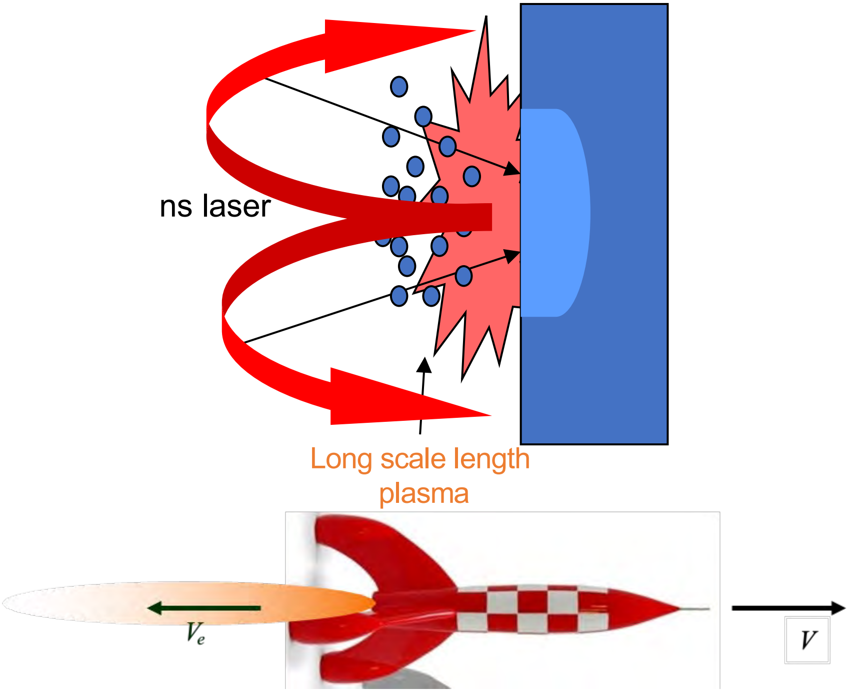
NEED A POINT X-RAY SOURCE

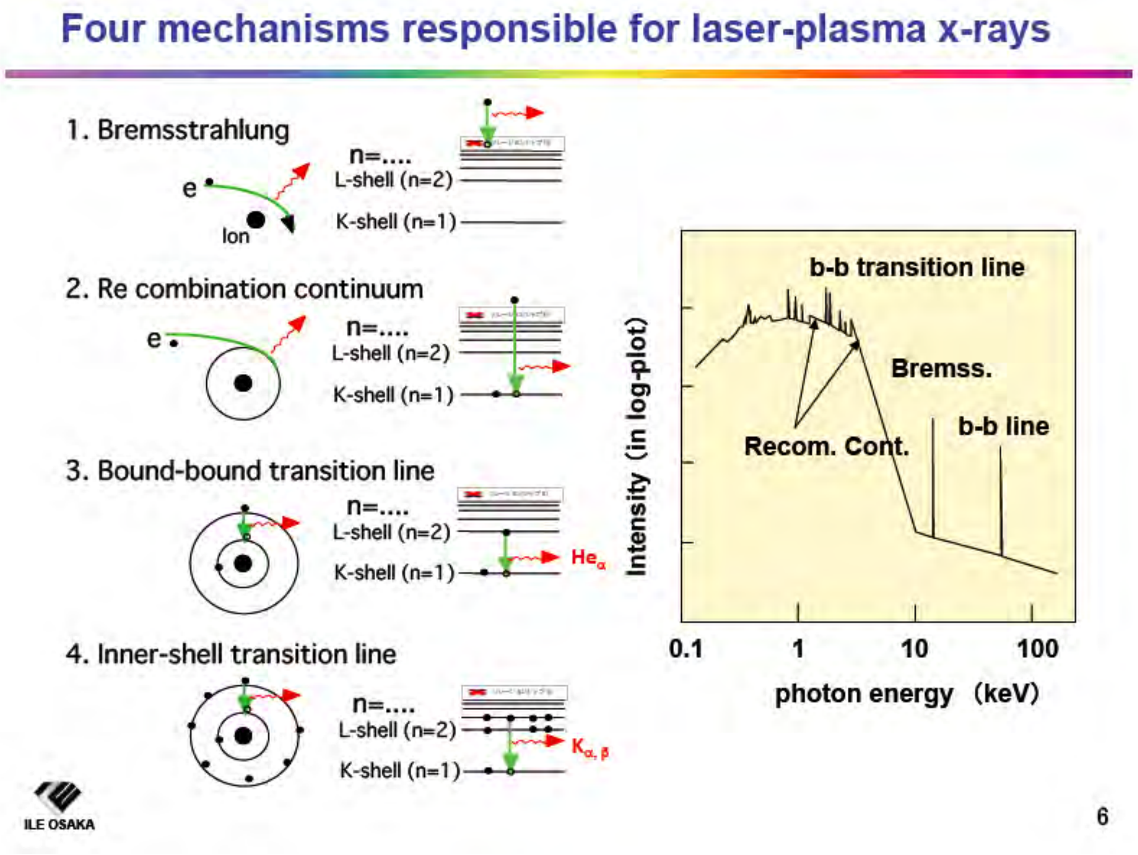
1970 – 1989: VERY LARGE X-RAY SOURCE SIZE

✓ mid 70's :

- *Nd glass lasers (NRL, LLE, CEA, LLNL, X, Rutherford…)*
- *CO2 lasers (LANL, NRC, INRS, Osaka…)*

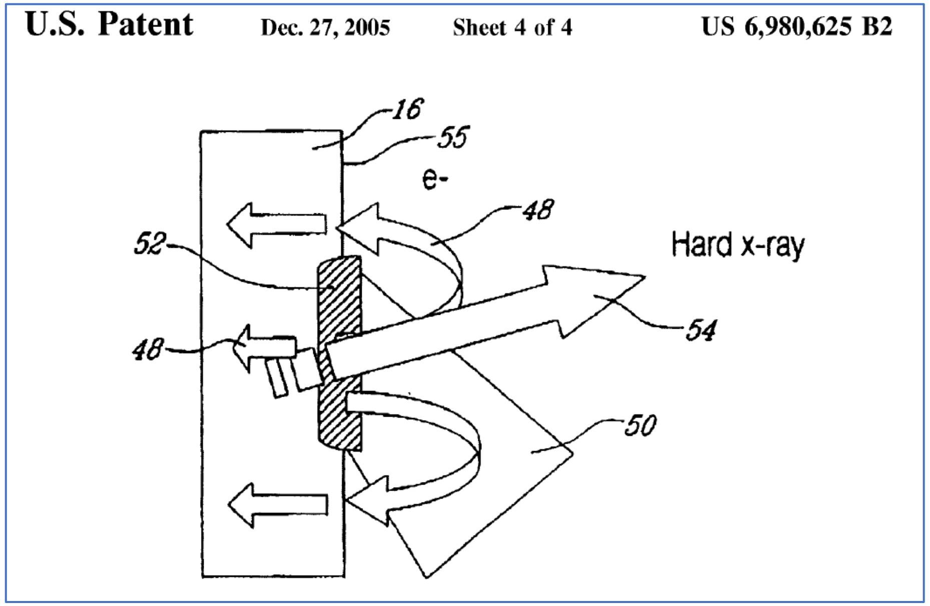
  Hot electrons, Hard x-rays,
  e and ion acceleration, B fields AND lateral transport

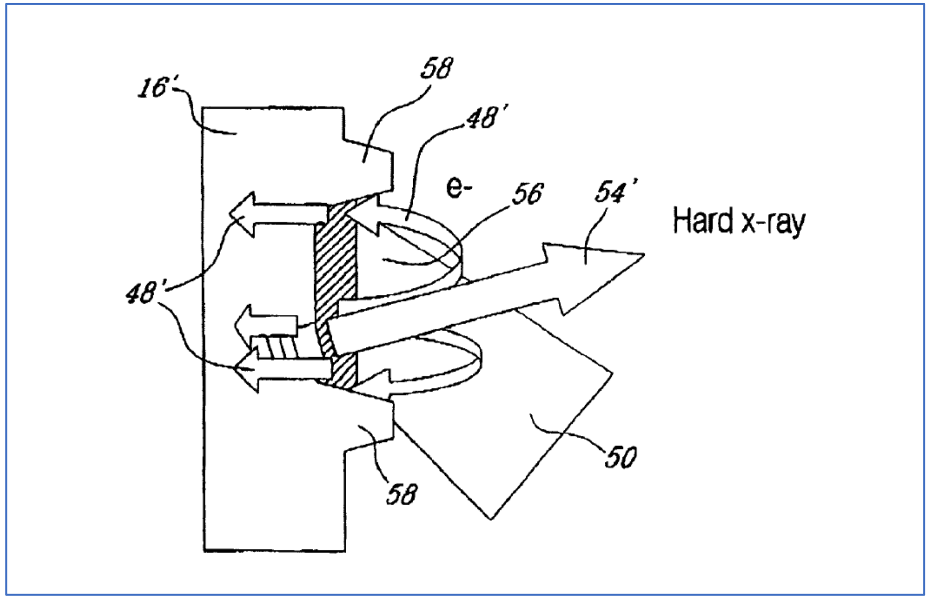




NEED A POINT X-RAY SOURCE

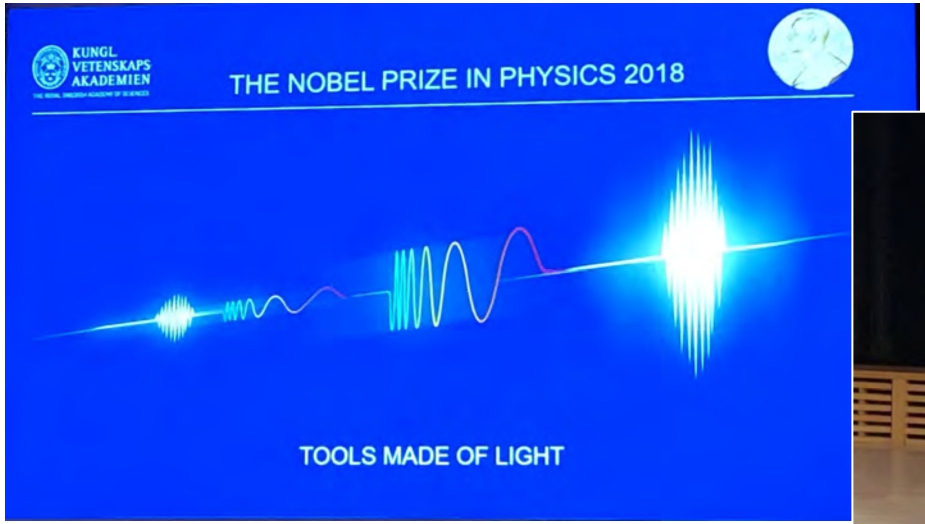
1970 – 1989: VERY LARGE X-RAY SOURCE SIZE





A FIRST REVOLUTION

1985: Donna Strickland & Gérard Mourou :
The energy stacked in a very short time



Opt. Communication 56, 219 (1985)

1989: Matter heated on a time scale shorter than dynamics

DOING SHORT IN TIME ALLOWS TO DO SMALL IN SPACE

VOLUME 62, NUMBER 7 PHYSICAL REVIEW LETTERS 13 FEBRUARY 1989

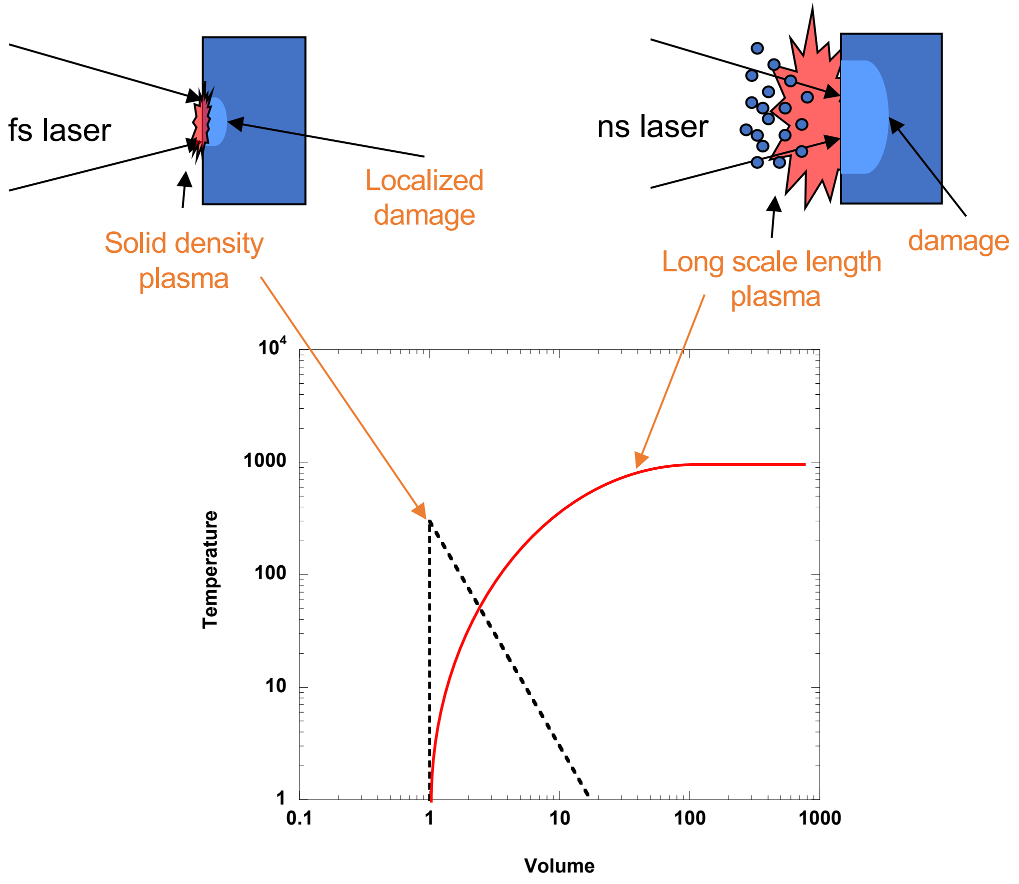
Short-Pulse Laser Absorption in Very Steep Plasma Density Gradients

J. C. Kieffer,[a] P. Audebert, M. Chaker, J. P. Matte, H. Pépin, and T. W. Johnston
Institut National de la Recherche Scientifique–Energie, Université du Québec, 1650, montée Ste-Julie, Varennes, Québec, Canada J0L 2P0

P. Maine, D. Meyerhofer, J. Delettrez, D. Strickland, P. Bado, and G. Mourou
Laboratory for Laser Energetics, University of Rochester, Rochester, New York 14620
(Received 25 October 1988)

We have measured the absorption of 1-ps laser pulses interacting with matter at intensities from 10^{10} to 10^{16} W/cm^2. The variations of absorption with incidence angle and polarization have been used to infer submicron plasma-density-gradient scale lengths. The results show a transition between a regime of laser interaction with sharply bounded dense cold matter ($I \le 5\times10^{12}$ W/cm^2), where absorption is by the usual skin depth effect, to a regime of interaction with a plasma of very steep density gradient ($L/\lambda \le 0.2$) (5×10^{12} W/cm$^2 \le I \le 10^{15}$ W/cm^2).

PACS numbers: 52.40.Nk, 52.25.Rv, 52.50.Jm

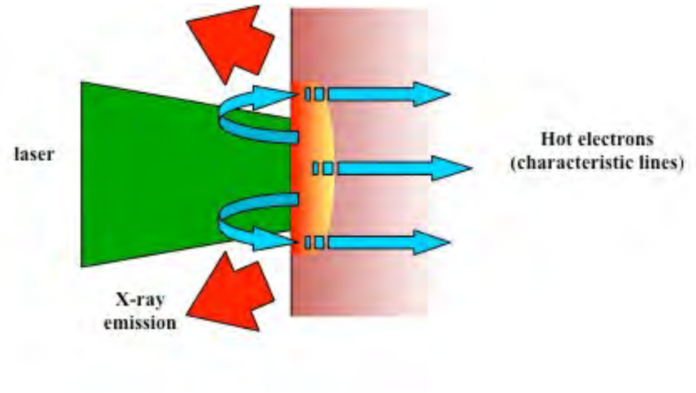


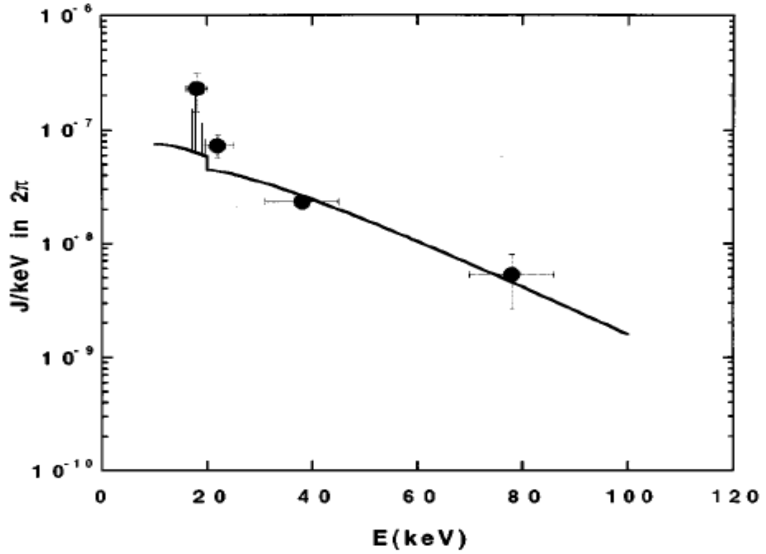
NEED A POINT X-RAY SOURCE

1989 – 2023 K-alpha X-ray source

✓early 90's:

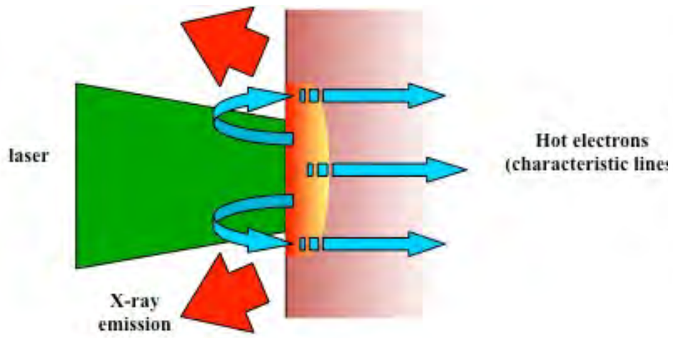
- *proposals by Lundt and INRS-SUNY for the application of ultrafast laser-based x-ray sources to medical imaging*



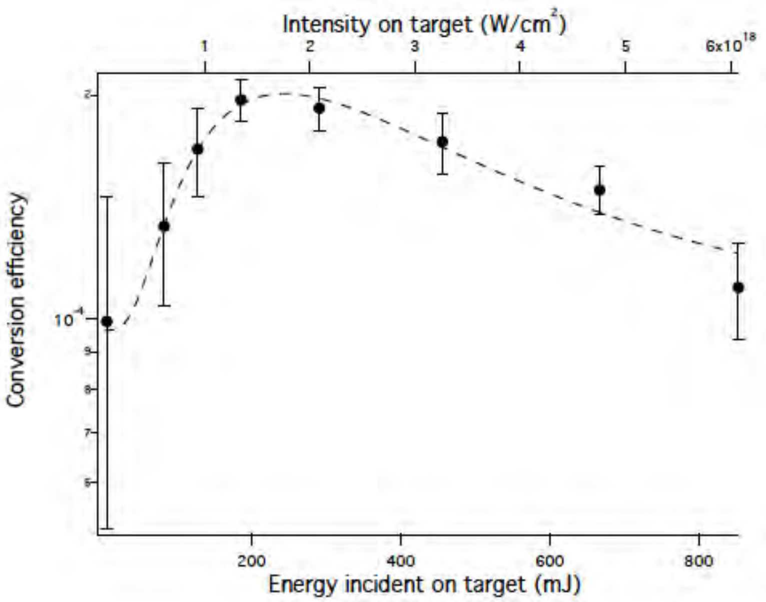


NEED A POINT X-RAY SOURCE

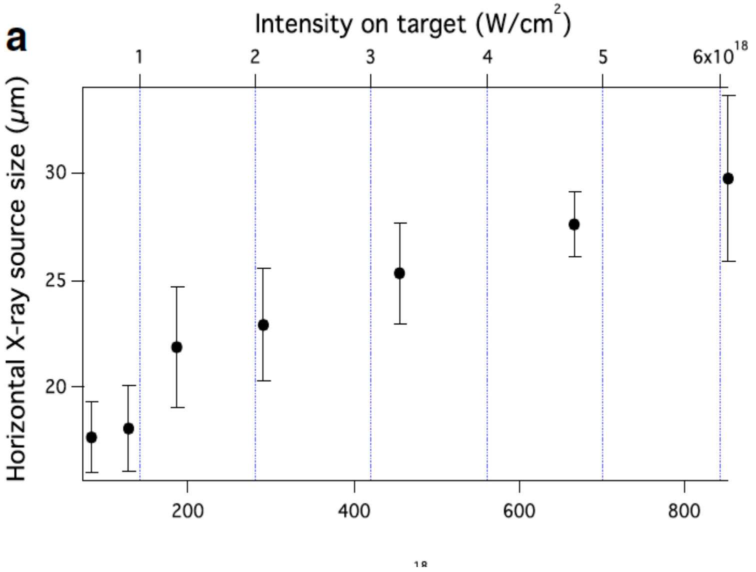
1989 - 2023



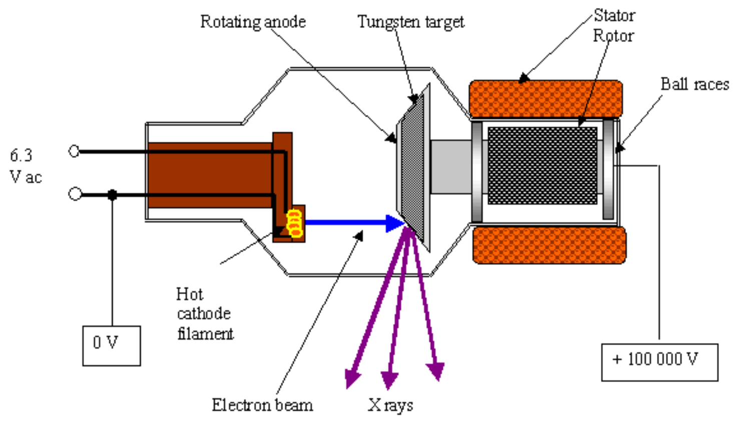
10^{-4} efficiency at 17keV (Mo)

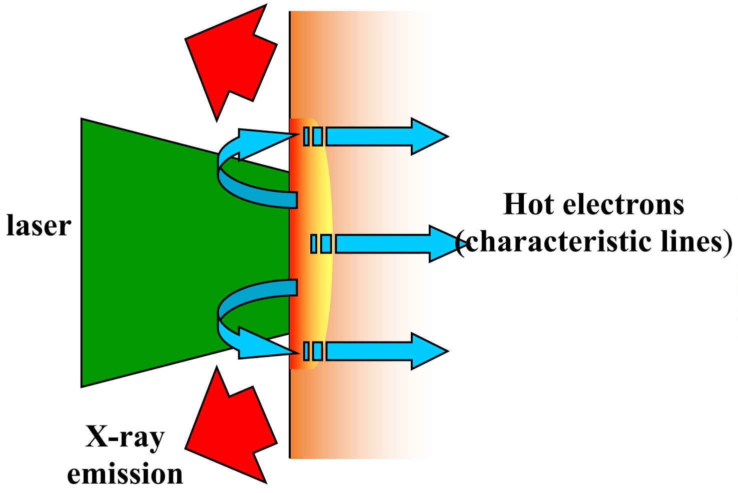


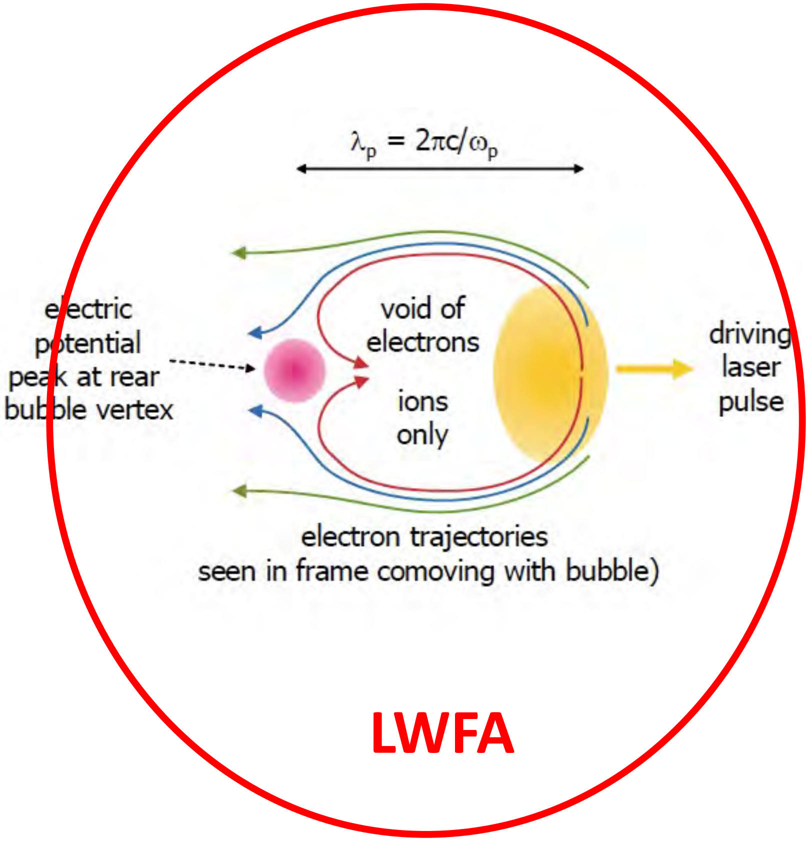
20µm source size at 17keV (Mo)



Is there a future for a laser-based X-rays?



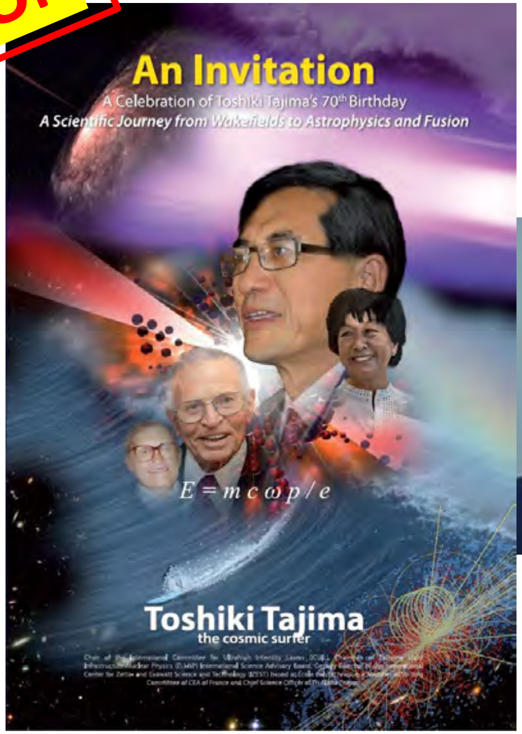




ALLS
Advanced Laser Light Source

From the concept to the electron dream beam

A SECOND REVOLUTION



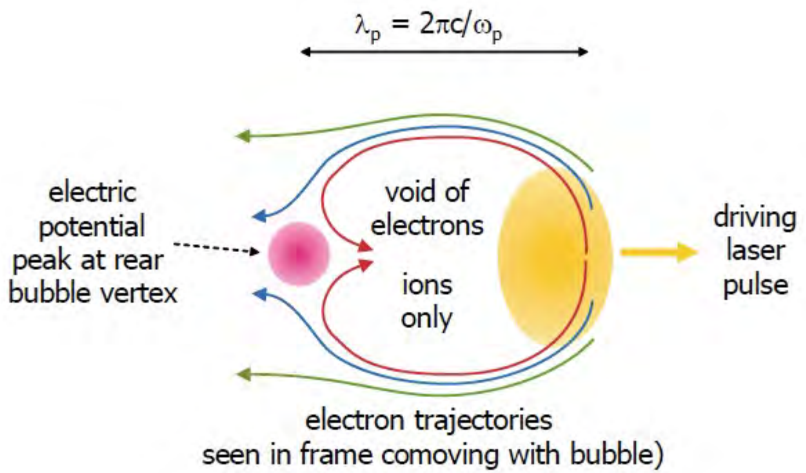
Eric Esarey

Victor Malka

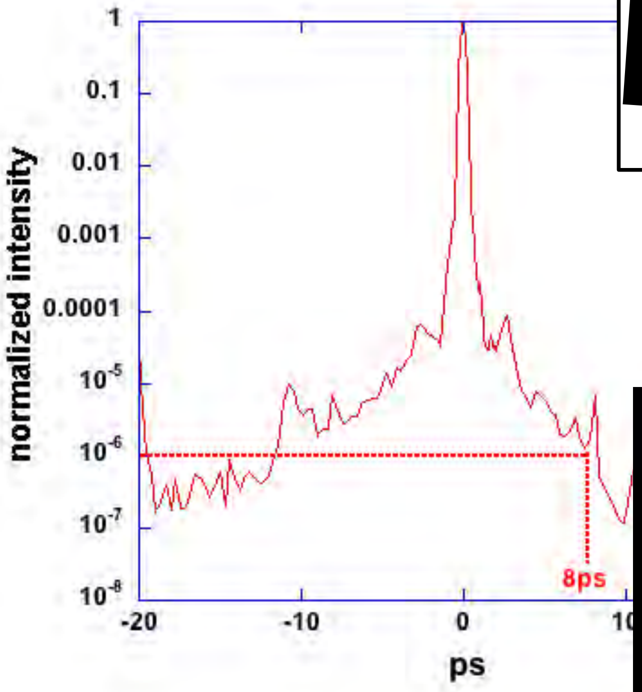
1979

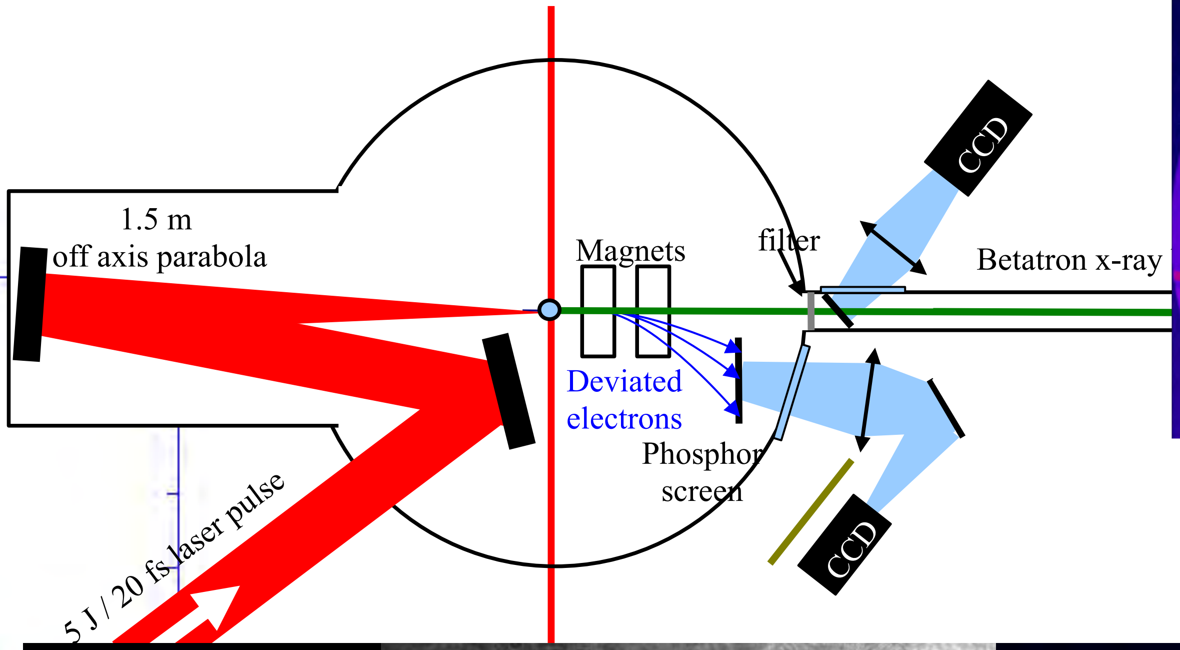
2004

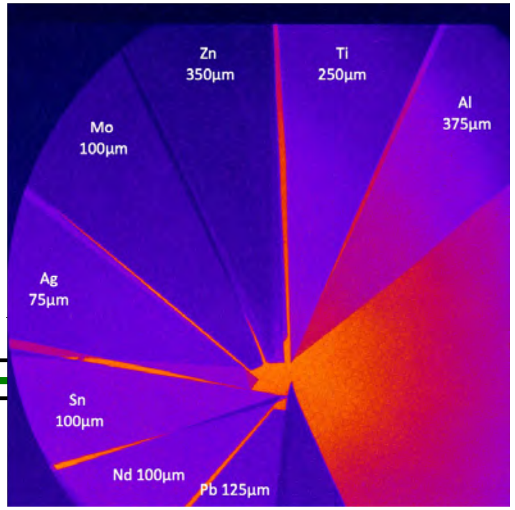
Accelerating electrons

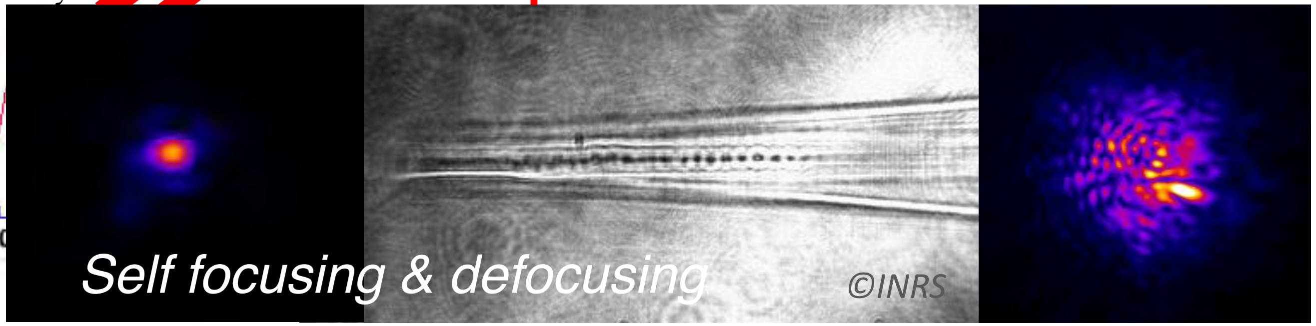


More complex with a real laser

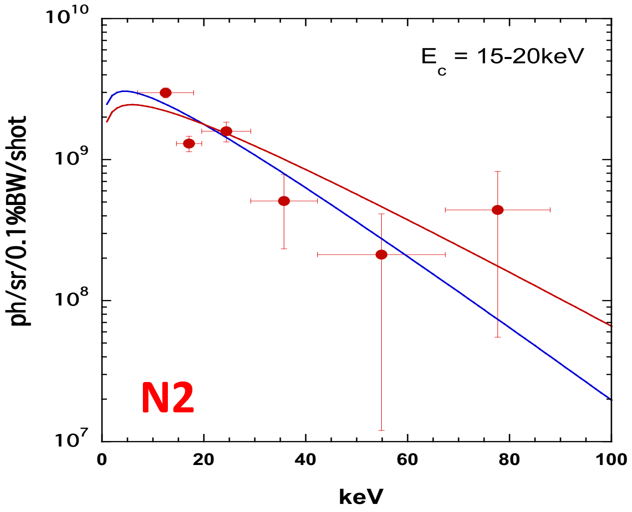


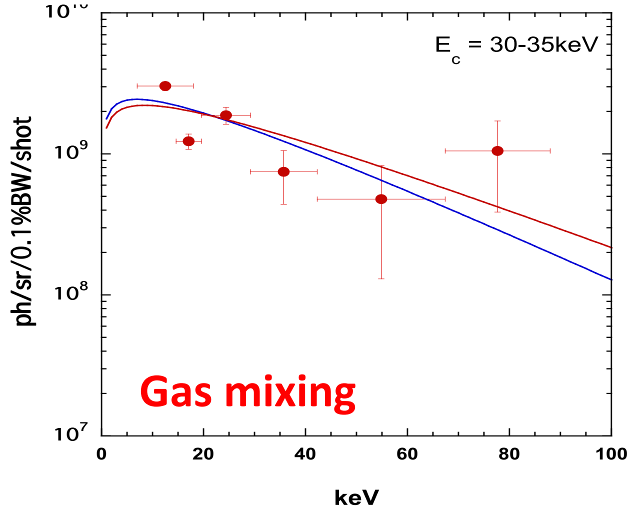






The X-ray emission





New Journal of Physics
The open-access journal for physics

Demonstration of the synchrotron-type spectrum of laser-produced Betatron radiation

S Fourmaux[1,4], S Corde[2], K Ta Phuoc[2], P M Leguay[1], S Payeur[1], P Lassonde[1], S Gnedyuk[1], G Lebrun[1], C Fourment[3], V Malka[2], S Sebban[2], A Rousse[2] and J C Kieffer[1]

[1] INRS-EMT, Université du Québec, 1650 Lionel Boulet, Varennes J3X 1S2, Québec, Canada
[2] Laboratoire d'Optique Appliquée, ENSTA ParisTech—CNRS UMR7639—École Polytechnique ParisTech, Chemin de la Hunière, Palaiseau F-91761, France
[3] Centre Lasers Intenses et Applications (CELIA), Université de Bordeaux-CNRS-CEA, Talence F-33405, France
E-mail: fourmaux@emt.inrs.ca

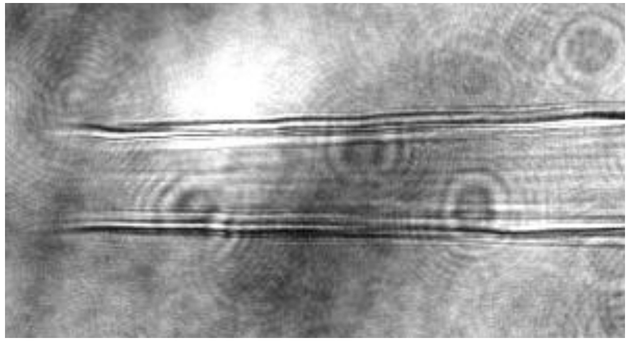
Research Article | Vol. 28, No. 3 / 3 February 2020 / *Optics Express* 3147
Optics EXPRESS

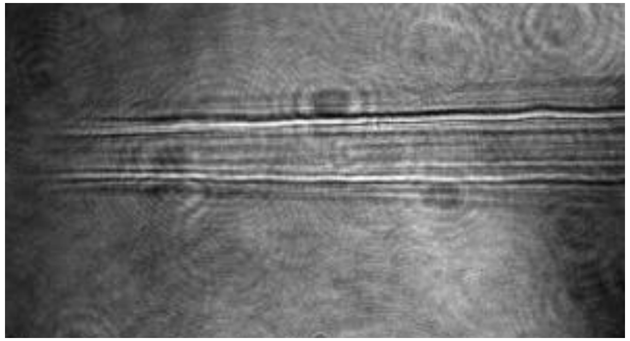
Laser-based synchrotron X-ray radiation experimental scaling

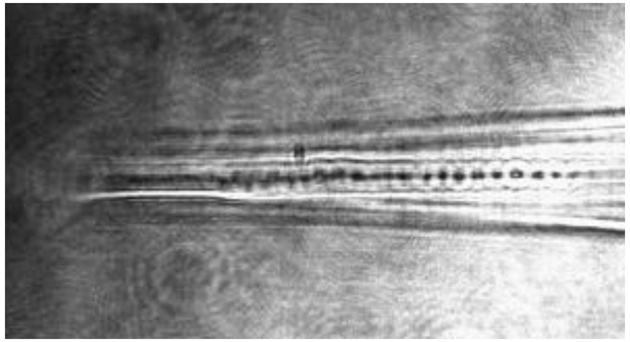
S. Fourmaux,[1,*] E. Hallin,[2] U. Chaulagain,[3] S. Weber,[3] and J. C. Kieffer[1]

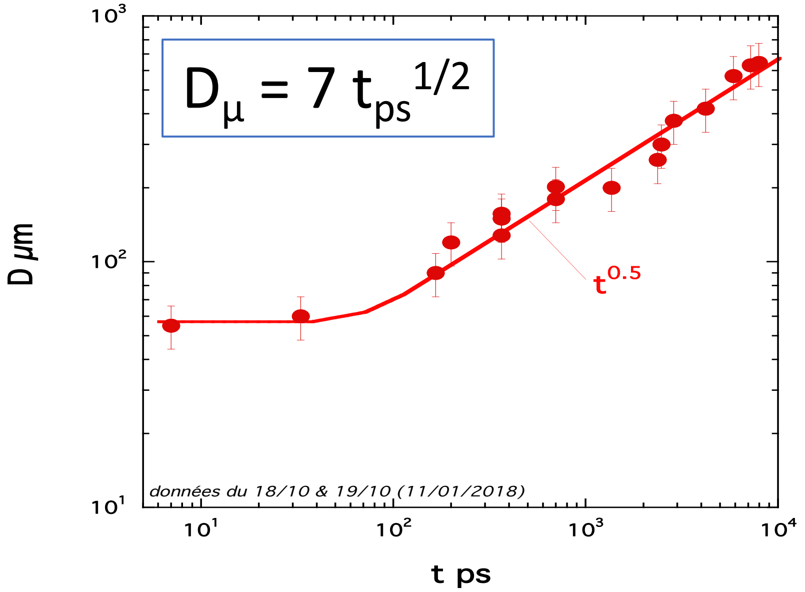
[1] Institut National de la Recherche Scientifique - Énergie, Matériaux et Télécommunications, Université du Québec (INRS-EMT), 1650 Lionel Boulet, Varennes J3X 1S2, Québec, Canada
[2] Global Institute for Food Security, 110 Gymnasium Place, University of Saskatchewan, Saskatoon S7N 4J8, Saskatchewan, Canada
[3] ELI Beamlines, Institute of Physics CAS, Prague 182 21, Czech Republic

The energy balance









Measured absorption = 2.3%

Incident energie = 3J

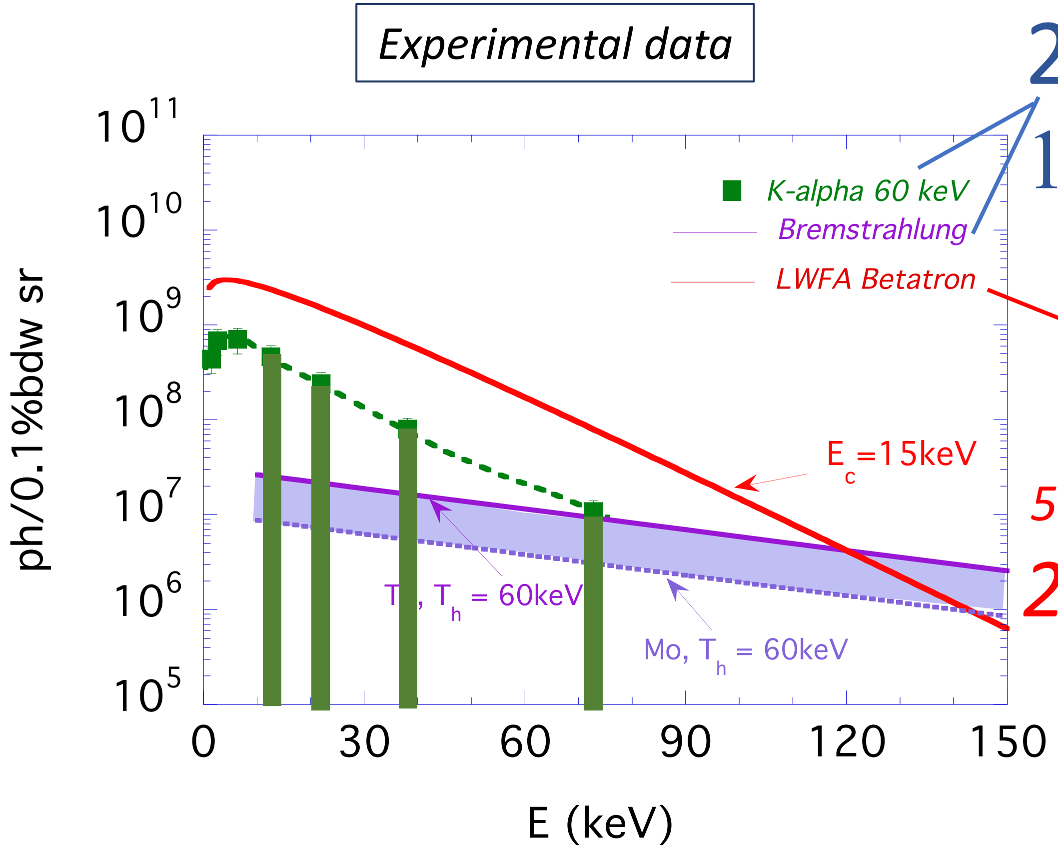
Energy in electron beam (150MeV – 350MeV) = 60mJ

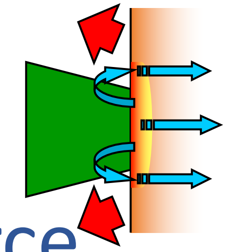
Energy in plasma (from the blast wave) = 10mJ

Energy in 10keV – 20keV X-ray beam = 20µJ

WHY LWFA ?

Bremstrahlung - K alpha - Betatron





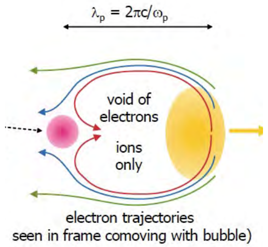
2π

15μm source

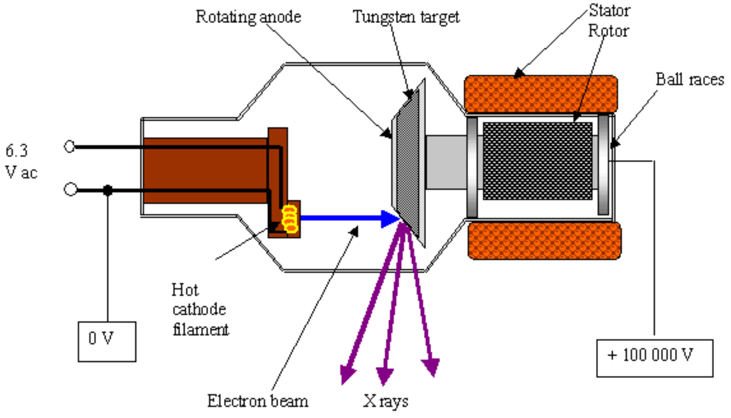
BEAM

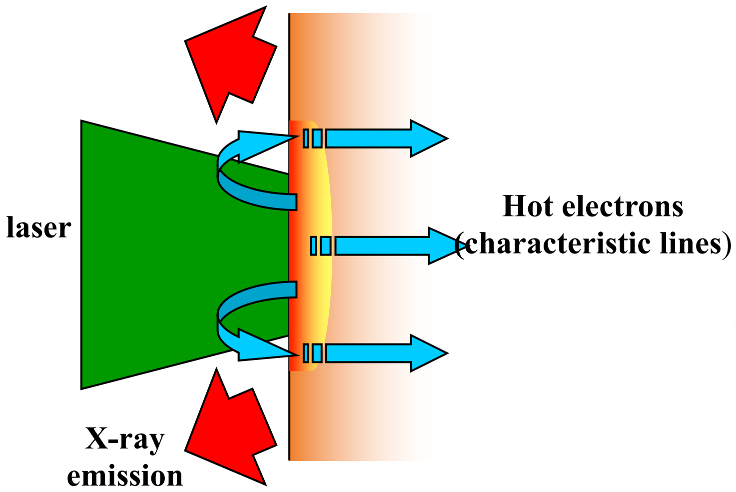
50mrad x 50mrad

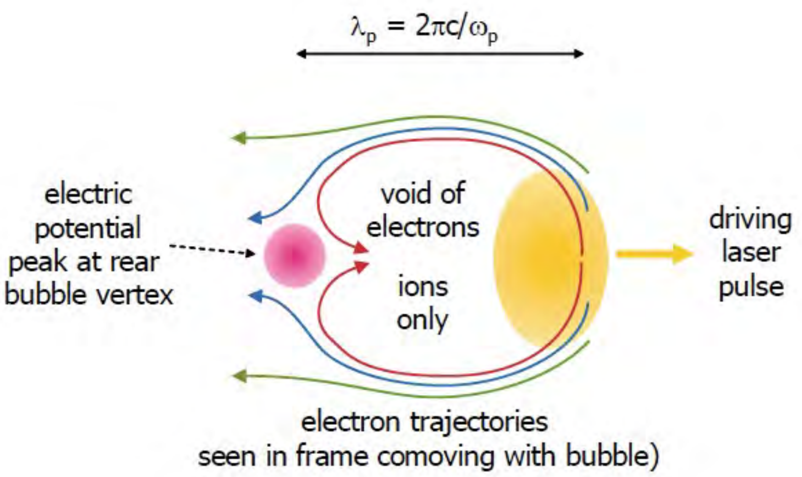
2μm source



Is there a future for a laser-based X-rays?







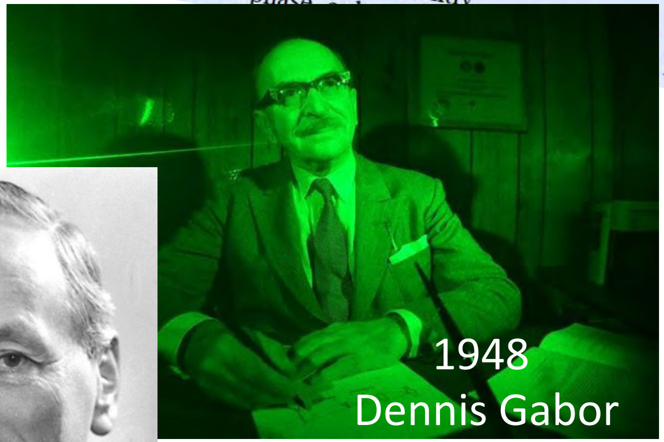
500µm **20µm** **1µm**

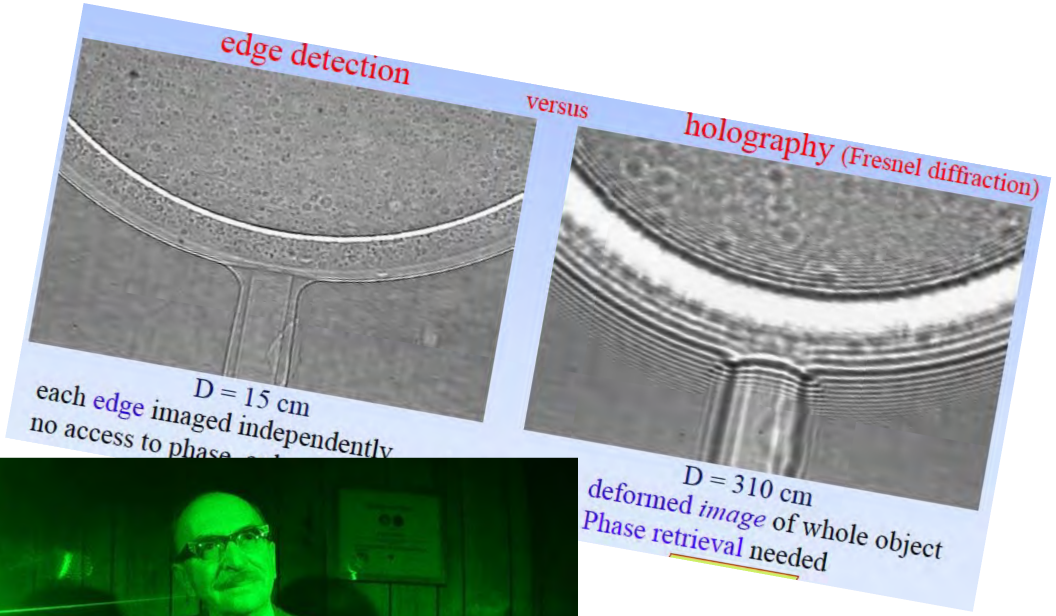
IMAGING & X-RAY HOLOGRAPHY

New way to image: X-ray holography

A THIRD REVOLUTION

1816
(Augustin Fresnel)

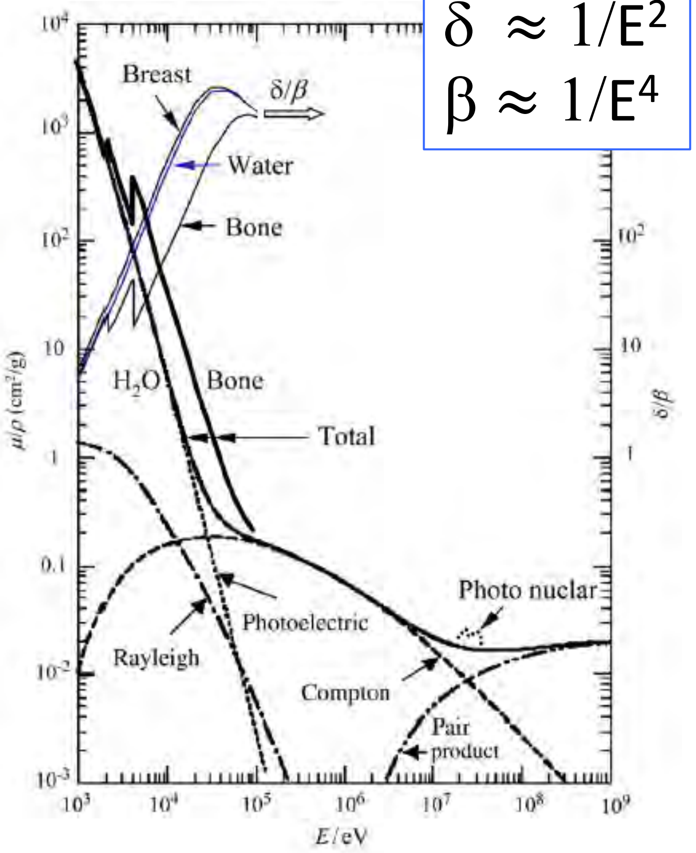




1995 (ESRF)

X-ray holography

- Complex index of refraction for x-rays: n = 1 - δ - iβ

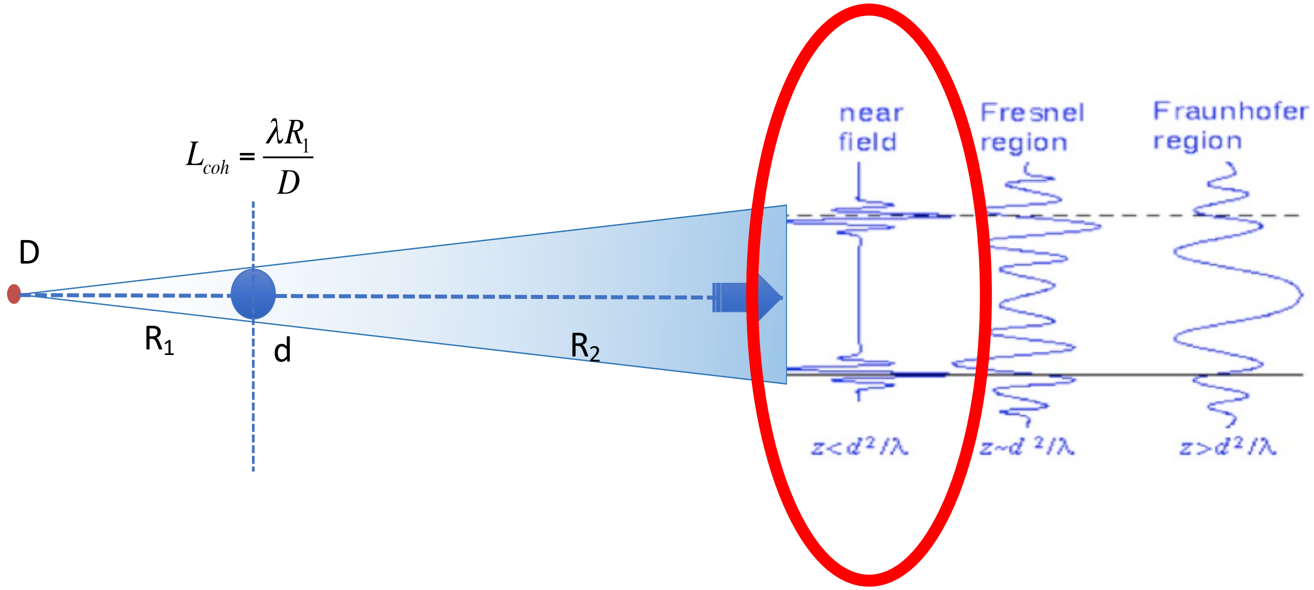


$\delta \approx 1/E^2$
$\beta \approx 1/E^4$

- 1933: Fritz Zernike: Phase contrast method
- 1948: Dennis Gabor's work on holography
- 1965: Ulrich Bonse and Michael Hart, Cornell University, New York.
  X-ray holography by cristal interferometry
- 1986: Abraham Szöke, LLNL : internal source Holographic microscopy
- 1995: Anatoly Snigirev, ESRF, propagation geometry and detection
  of Fresnel Fringes (similar to Denis Gabor set up)
- 1996: Wilkins et al, CSIRO, in line holography with microfocused X-ray tube

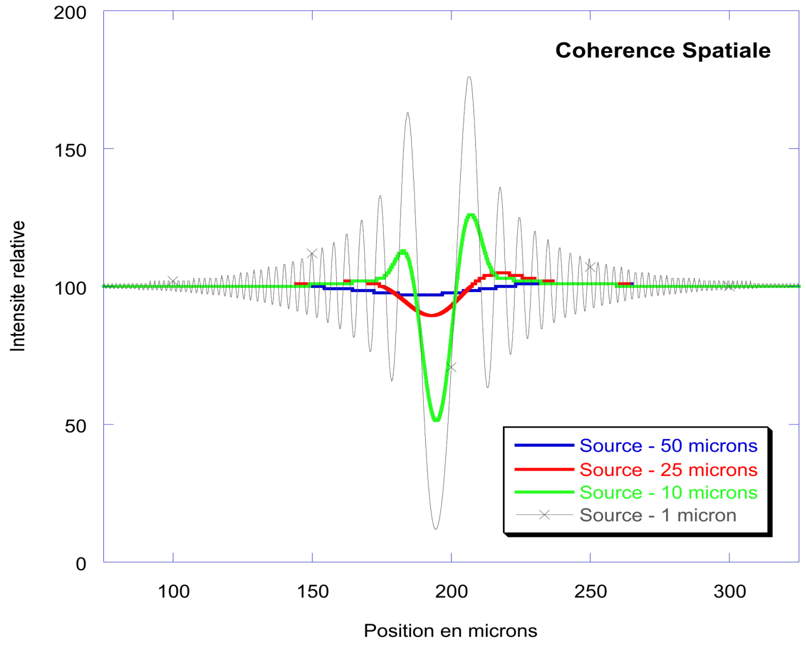
- 2004: INRS, first in line holography with laser based K-alpha sources
- 2011: INRS/LOA, First in line holography with laser betatron in real time
  (1 image in one shot)

In-line X-ray holography

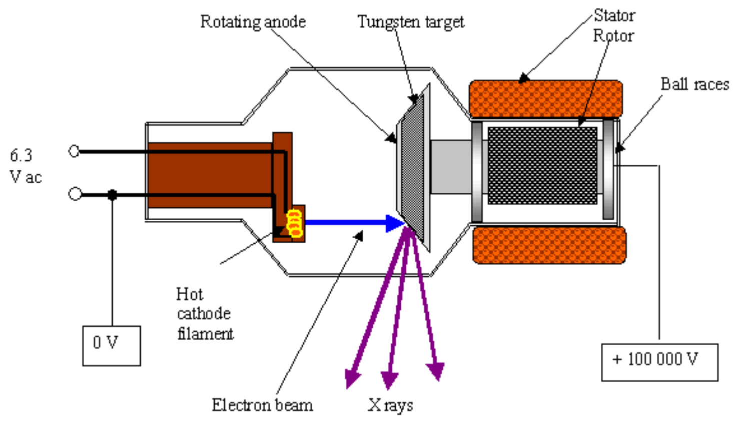


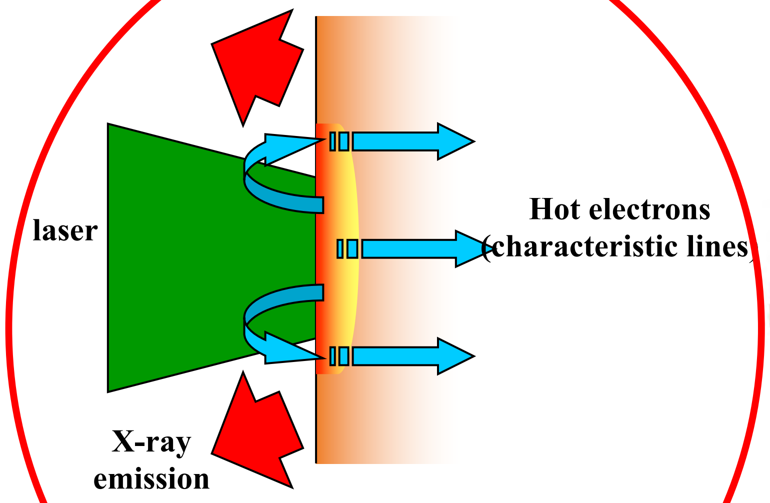
The diffraction pattern has to be above Poisson noise

X-ray sources size matters

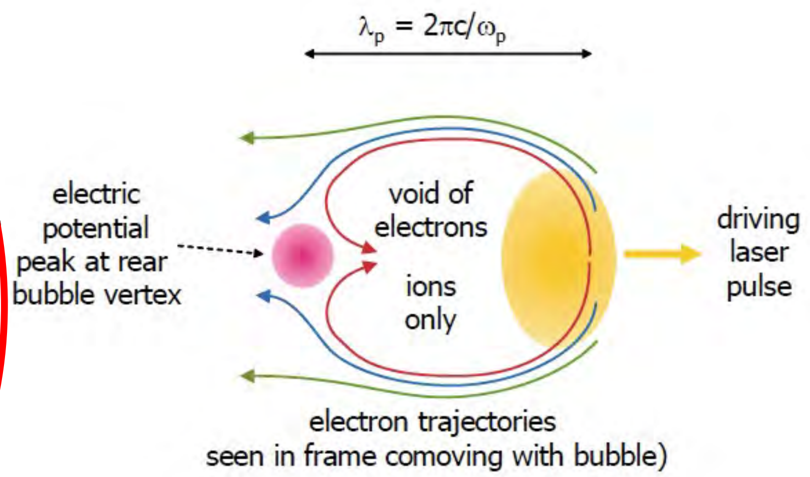


Is there a future for a laser-based X-rays?





1 image in 1s

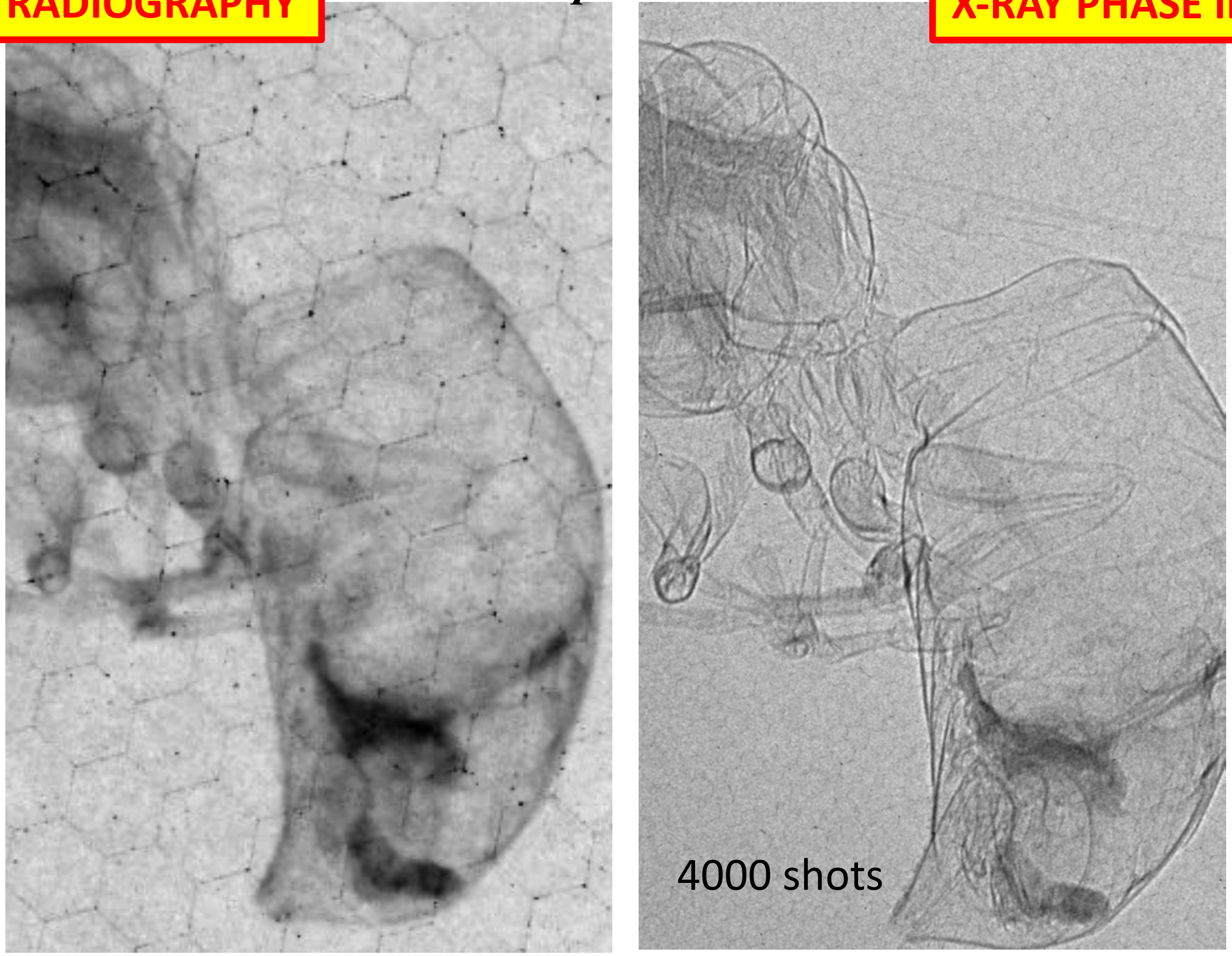


500µm **20µm** **1µm**

ALLS Advanced Laser Light Source

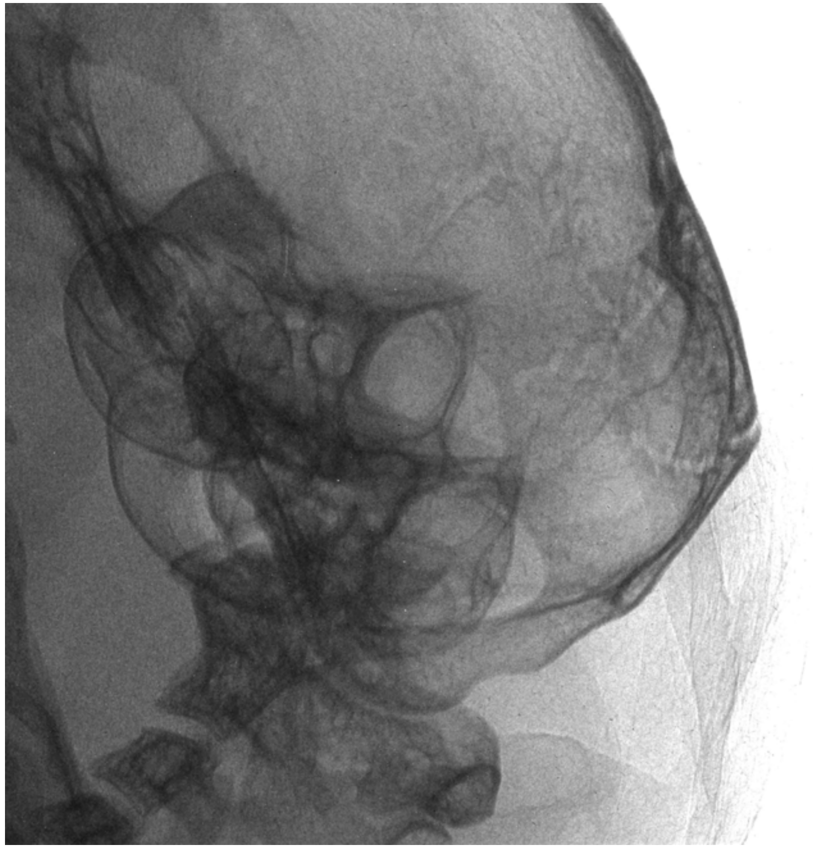
Laser-based X-ray Holography

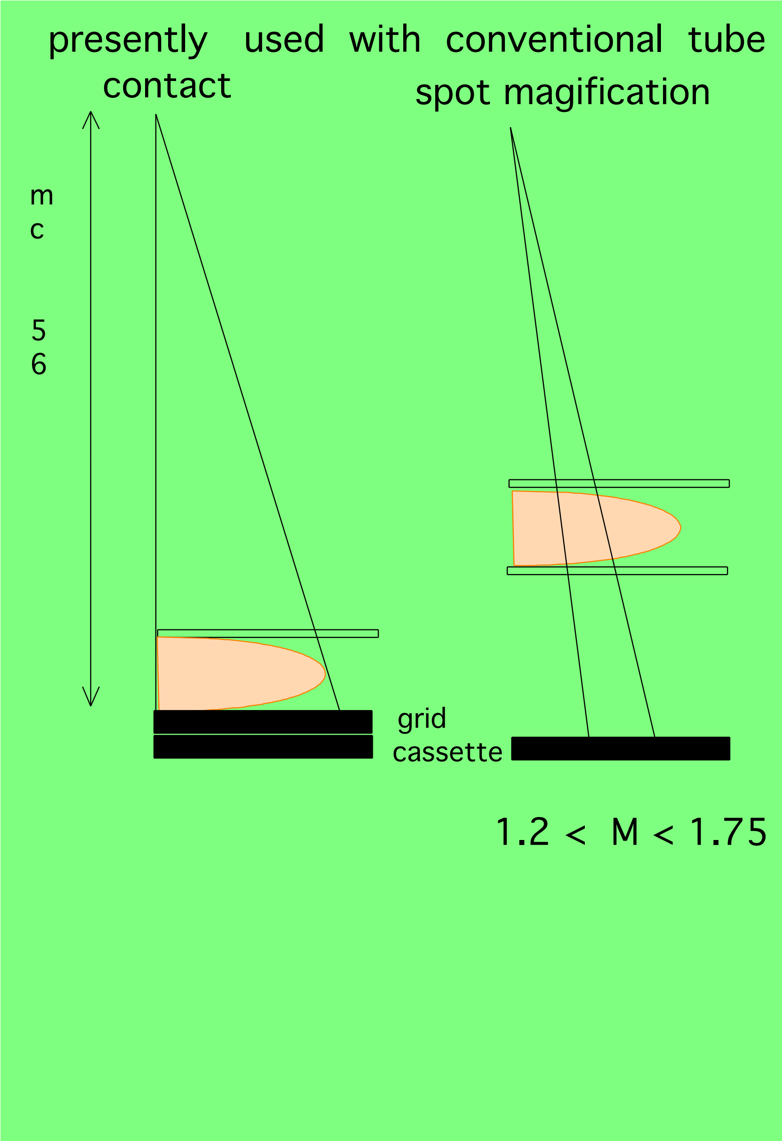
K-alpha 2005

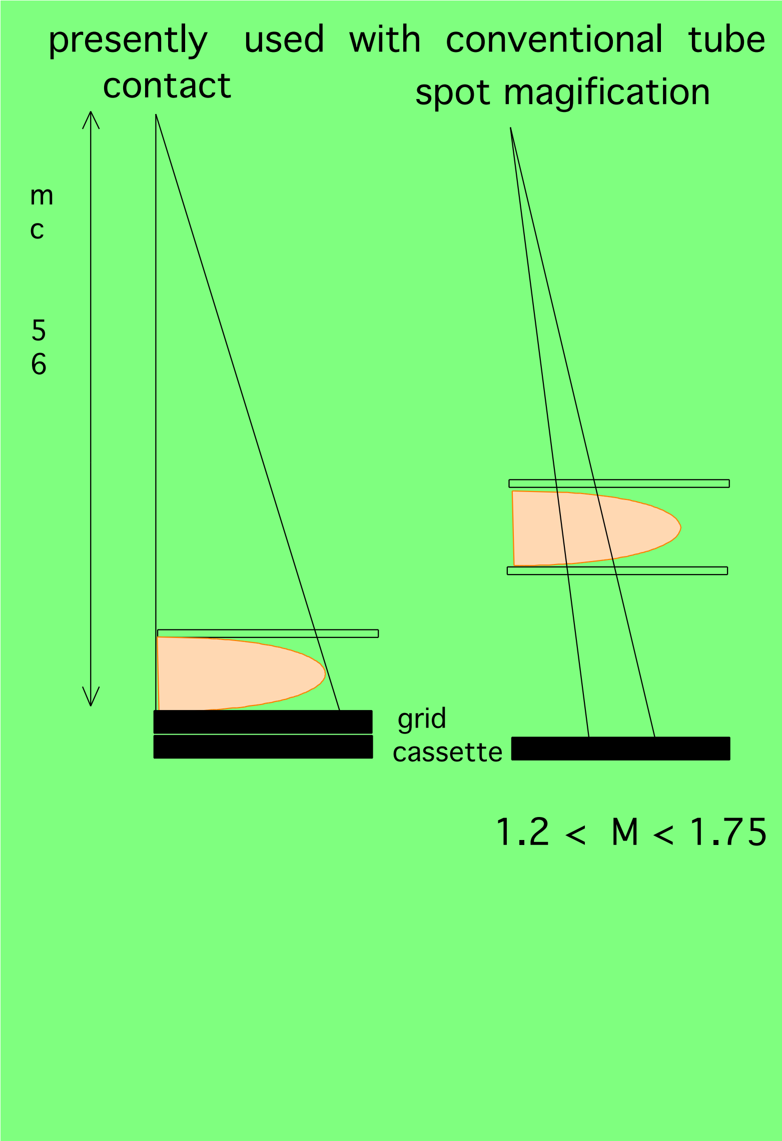


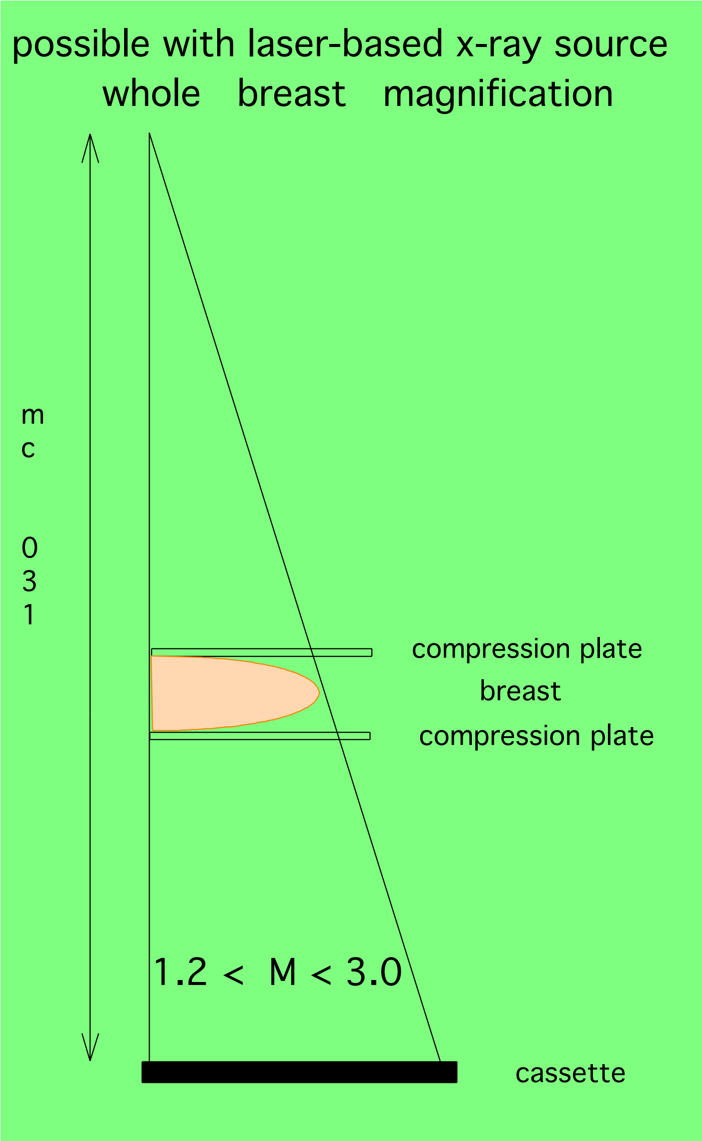
15µm X-ray source size
Monochromatic X-rays

2004: K-alpha radiation
The first demonstration of phase contrast imaging with Laser-based X-ray sources

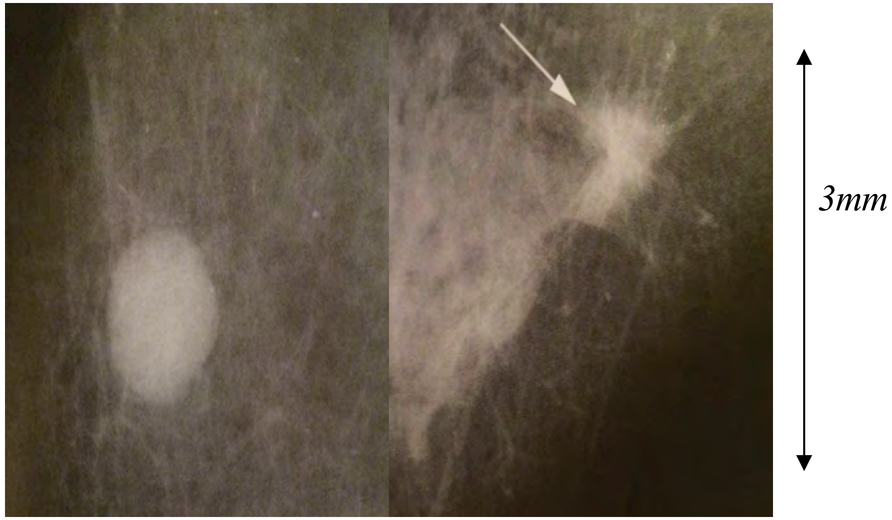


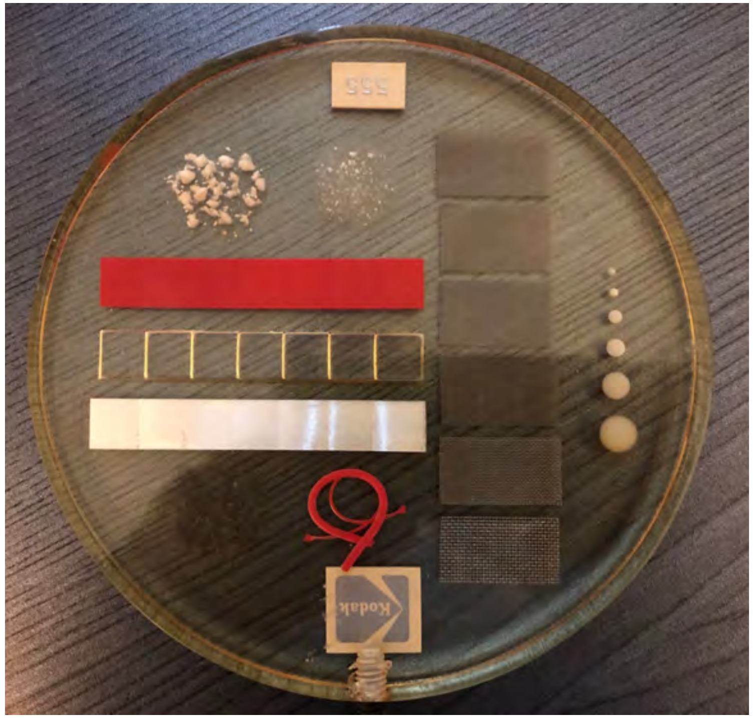

presently used with conventional tube
contact
spot magification
m
c
5
6
grid
cassette
1.2 < M < 1.75


presently used with conventional tube
contact
spot magification
m c 5 6
grid
cassette
1.2 < M < 1.75


possible with laser-based x-ray source
whole breast magnification
m c 0 3 1
compression plate
breast
compression plate
1.2 < M < 3.0
cassette

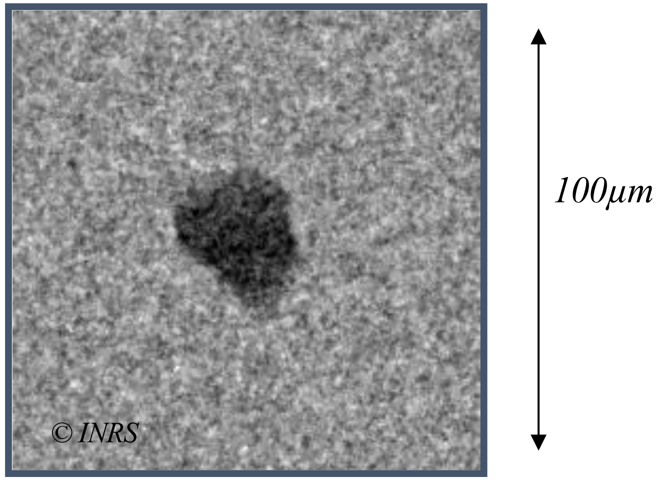
CONVENTIONAL vs LASER-BASED (solid target)



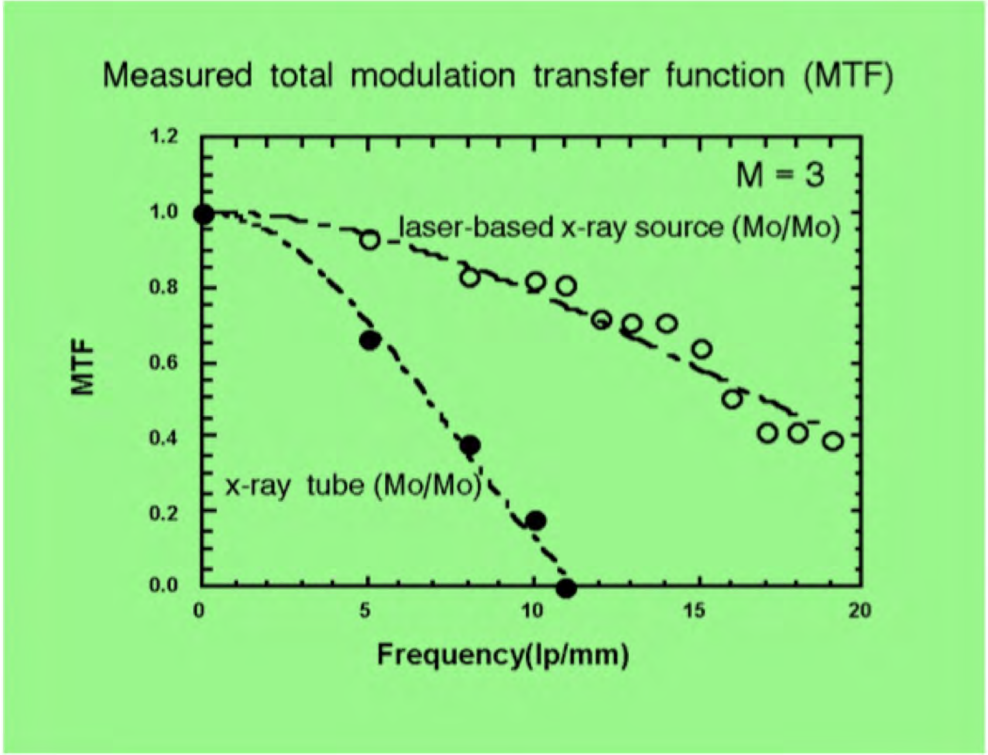


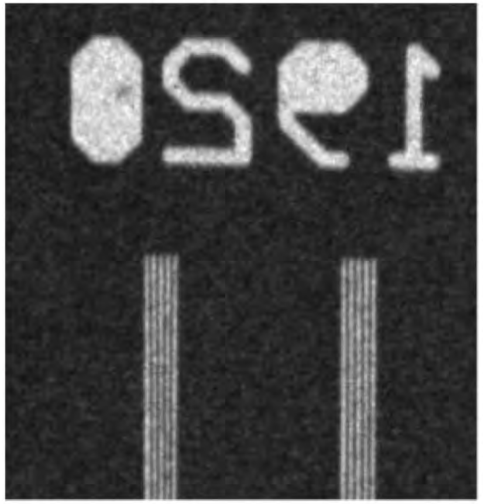
ITO Kodak Pathé 555
Polyester resin (1.3cm thick and density 1.25)

Successful demonstration



Imaging with Laser-based K-alpha X-ray sources





15μm source size

DOSE IS A CONCERN

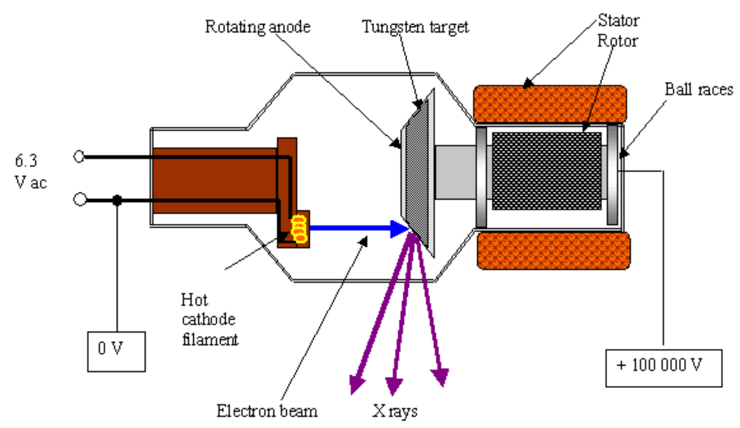
- What matters: the image quality or the patient safety ?
  - ✓ To obtain a very high image quality and an image giving the maximum of pertinent medical information, we need to increase the irradiation (dose)
- Where is trade-off between dose and pertinent information ?
  - ✓ Can we substantially decrease the dose and recover pertinent information thanks to the phase contrast (X-ray holography) ?

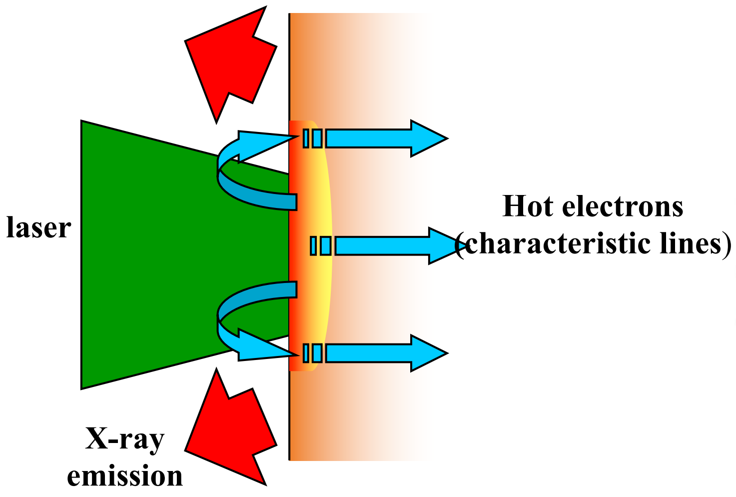
DOSE IS A CONCERN

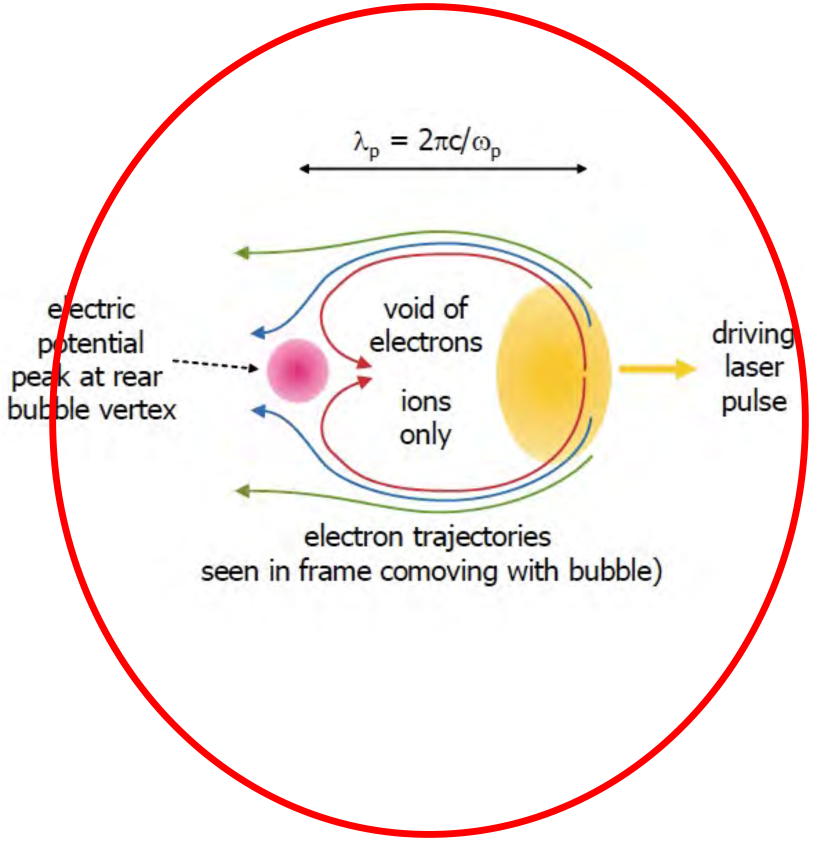
The idea is to relax the technical constraint by using a unique characteristic of the laser-based X-ray source

- An X-ray point source enable imaging with the X-ray phase (no absorption) and thus with minimum radiation deposition (dose) inside the tissues

Is there a future for a laser-based X-rays?





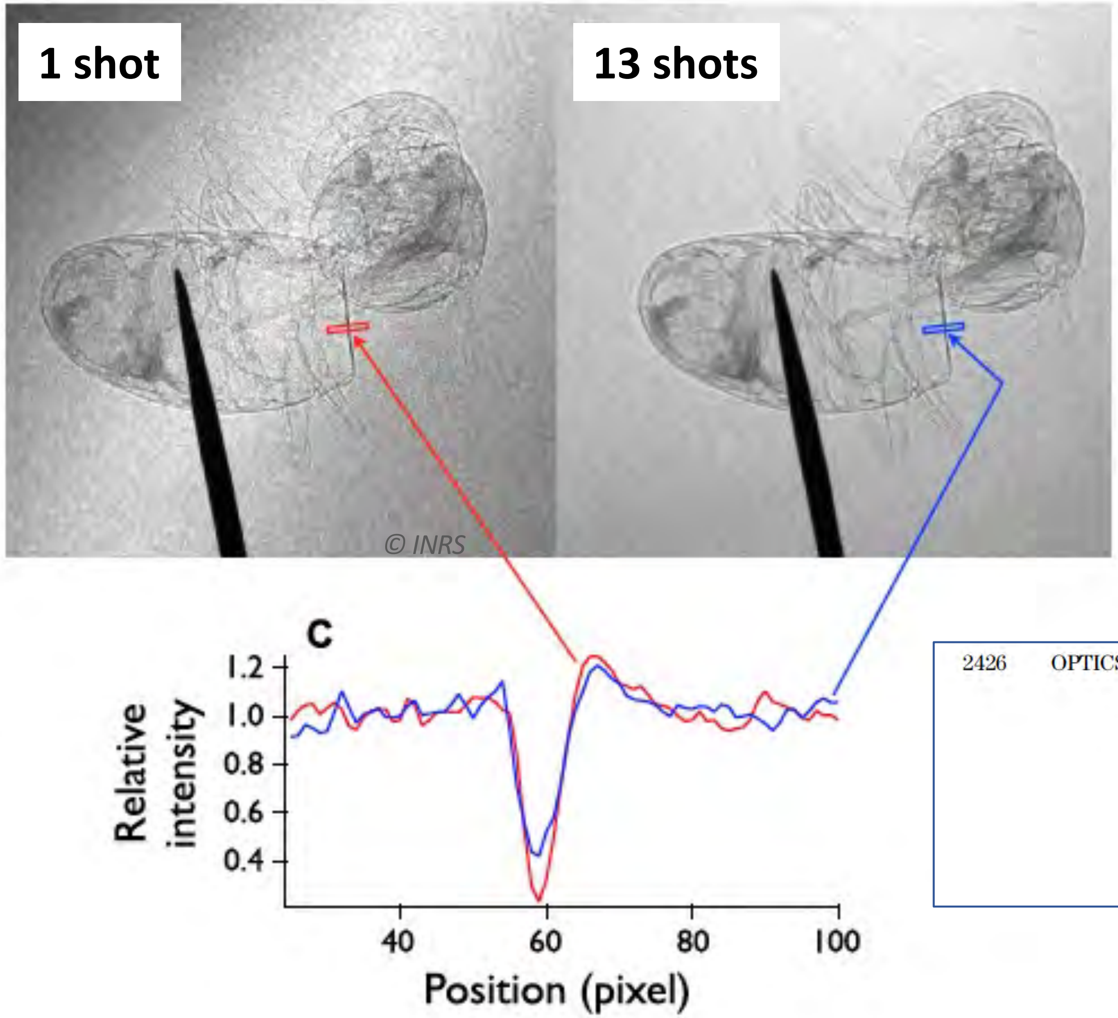


1 image in 1s

500µm **20µm** **1µm**

ALLS
Advanced Laser Light Source

A huge step with LWFA in 2011



12keV X-rays

1.7µm X-ray source diameter

15µm Imaging resolution

2426 OPTICS LETTERS / Vol. 36, No. 13 / July 1, 2011

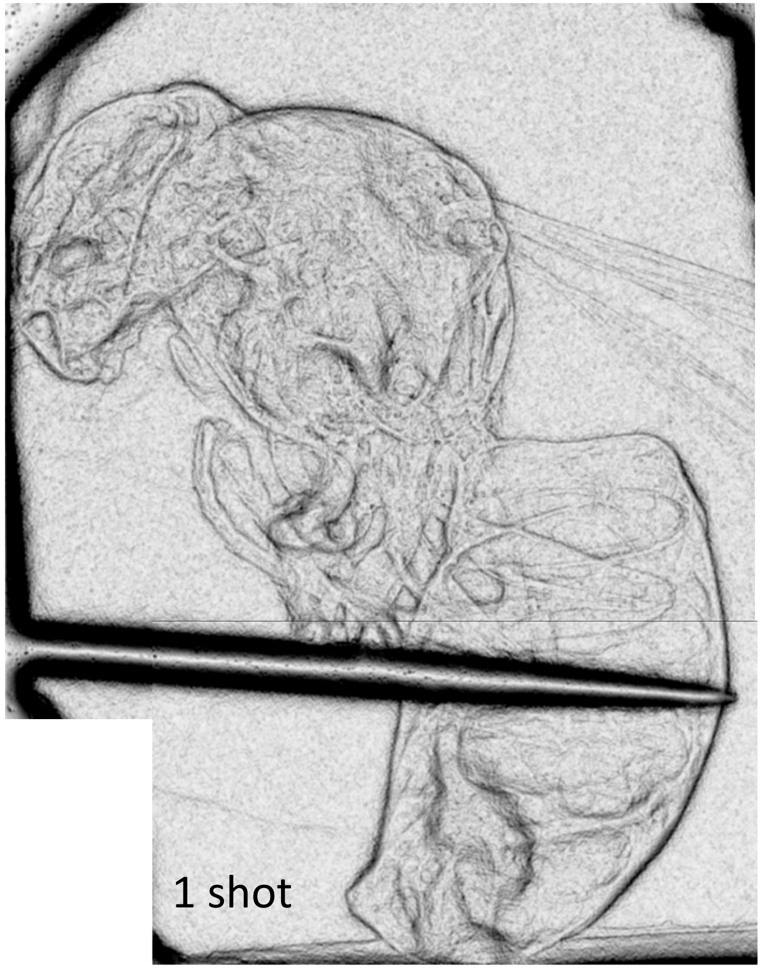
Single shot phase contrast imaging using laser-produced Betatron x-ray beams

S. Fourmaux,[1,*] S. Corde,[2] K. Ta Phuoc,[2] P. Lassonde,[1] G. Lebrun,[1] S. Payeur,[1] F. Martin,[1] S. Sebban,[2] V. Malka,[2] A. Rousse,[2] and J. C. Kieffer[1]

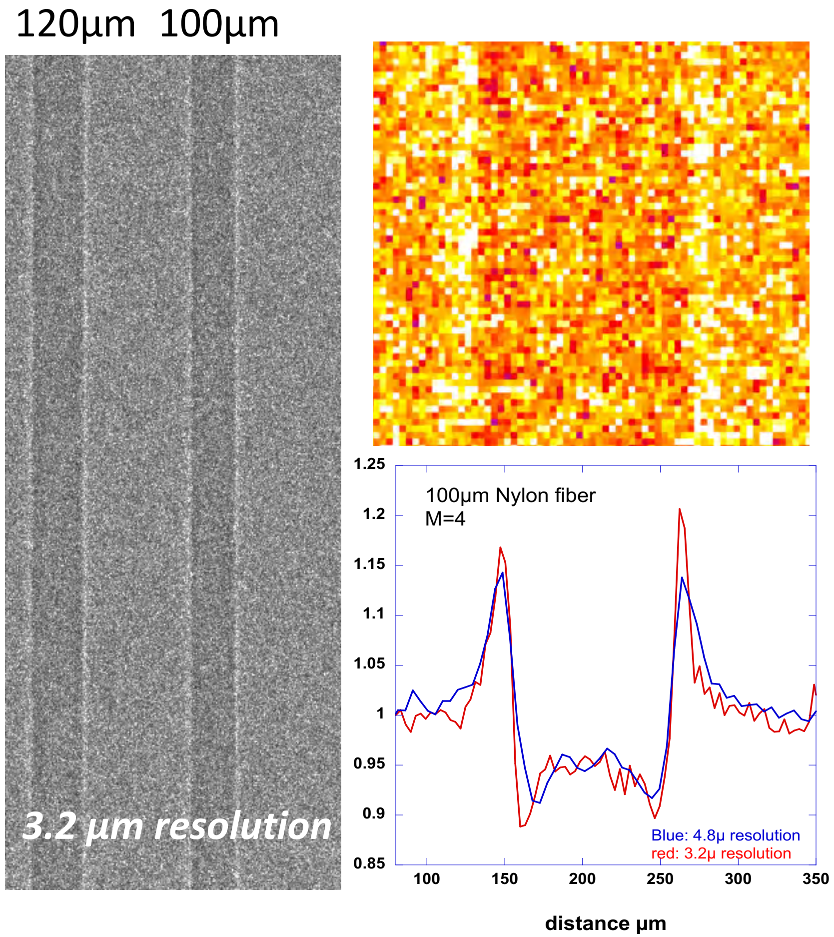
Laser-based X-ray Holography

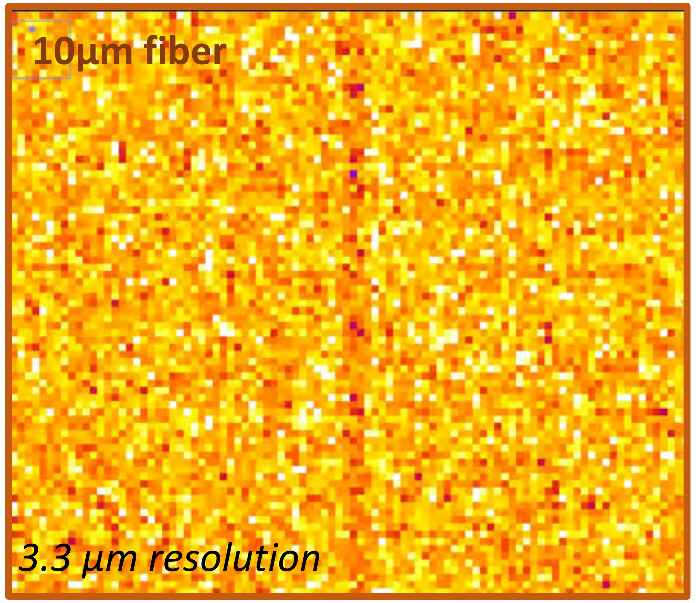
K-alpha 2005

LWFA 2011



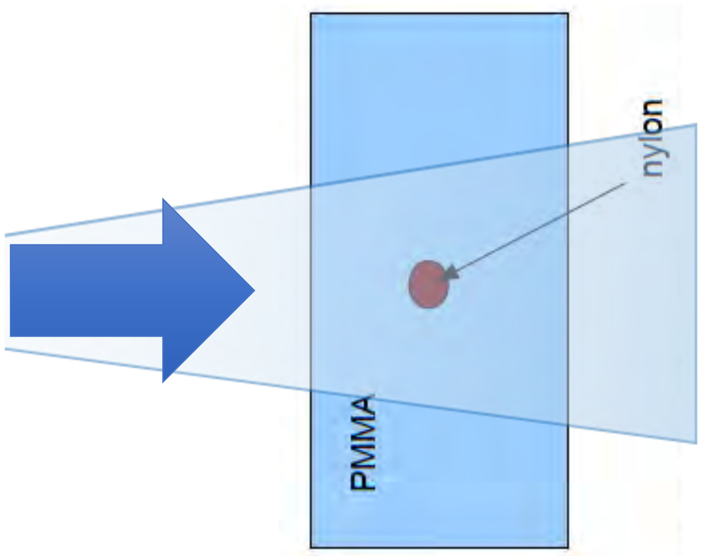
2022: Phase contrast imaging with 3µm resolution

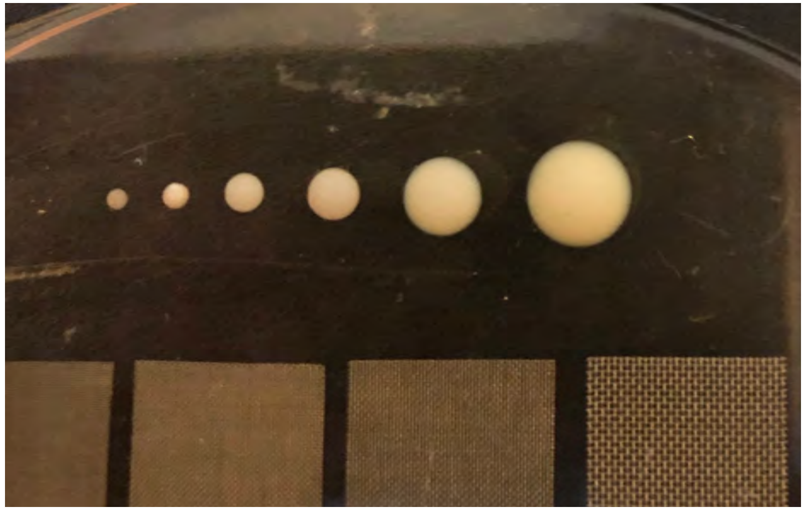




Pure phase image

Dose deposition at fixed image quality with phase contrast





Mammography phantom (ITO-Kodak)

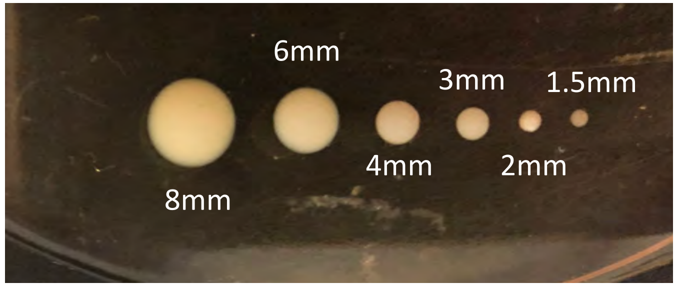
Nylon spheres (density 1.15) Embedded in a 1.3cm thick polyester resin (density 1.25)

Can this technology impact the medical & pre-clinical imaging market ?

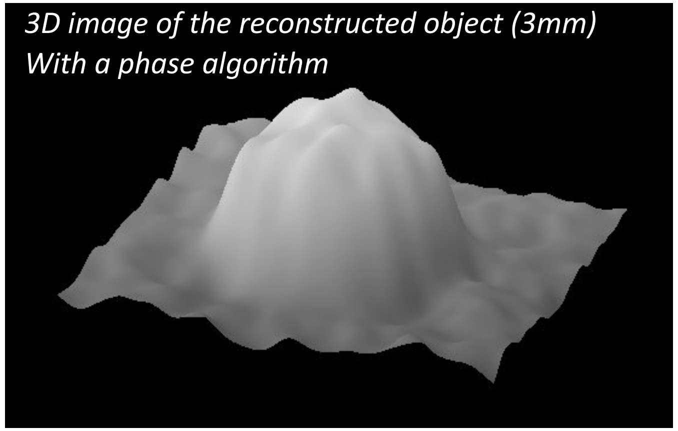
- Low dose breast cancer detection ?

- *Obtained with 1/10 of the clinical dose*

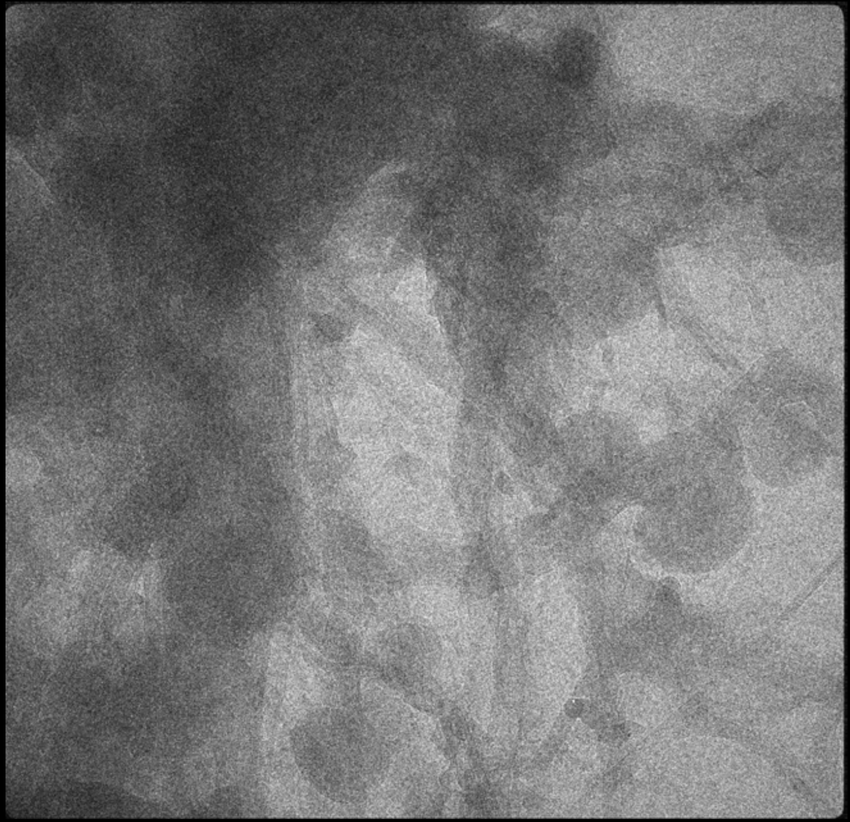
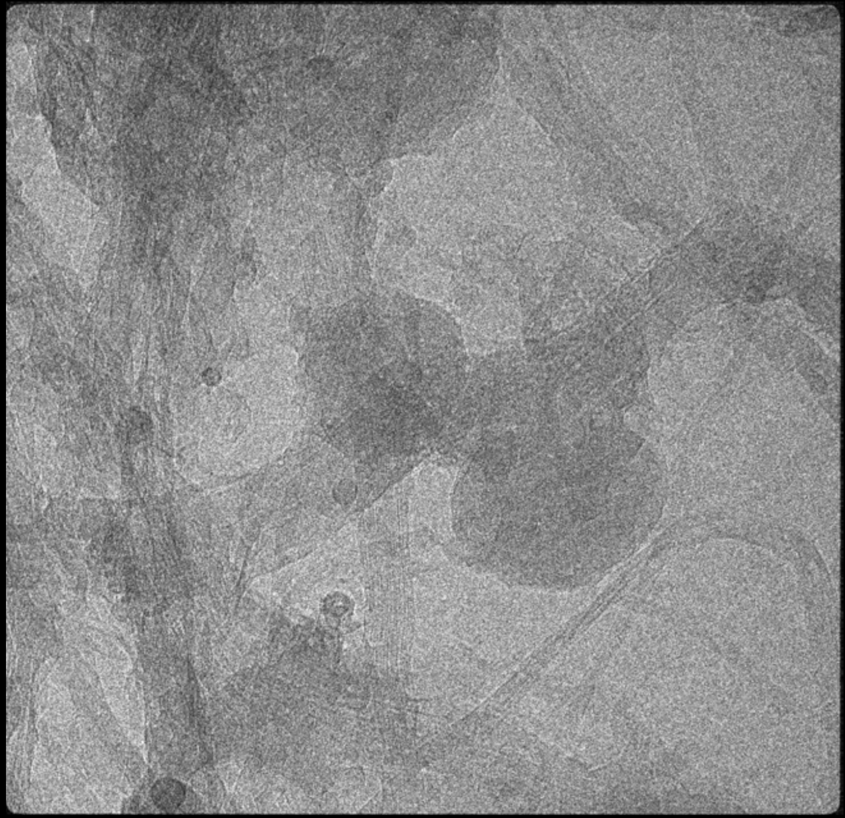
Mammography phantom



Obtained with 1/10 of the clinical dose



Disease monitoring in wheat fusarium (2013)


GIFS
GLOBAL INSTITUTE
FOR FOOD SECURITY



It is working in the laboratory but can we go inside an hospital or a farm ?

Bringing the machine inside the User world