HUNGARIAN NATIONAL LABORATORY

University of Szeged

Department of Oncotherapy
PI: Katalin Hideghethy

National Laser-initiated Transmutation Laboratory
PI: Karoly Osvay

NLTL National Laser-Initiated Transmutation Laboratory University of Szeged

Contribution to EuPRAXIA PP

HUNGARIAN NATIONAL LABORATORY

WP11 - Applications

Integrated Radiobiological Research, with the use of zebrafish models

Exploring laser-based neutron sources as a possible user station

WP12 – Laser technology

Development of diagnostics
Pilot experiment for testing new ideas
Component tests

National Laser-Initiated Transmutation Laboratory University of Szeged

University of Szeged

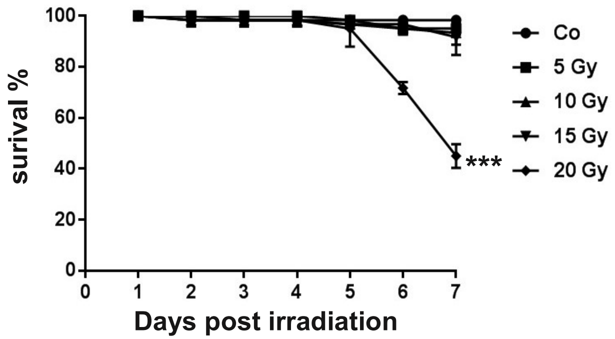
Department of Oncotherapy

Katalin Hideghethy’s group

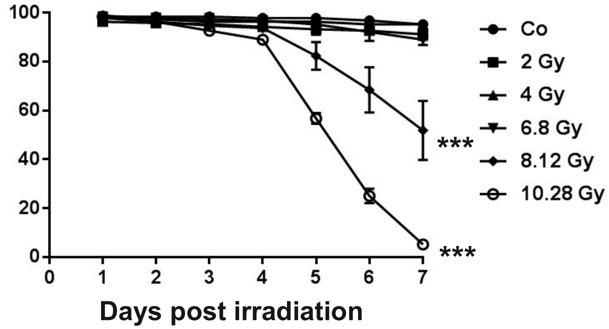
Previous and ongoing projects

Neutron RBE definition using ZF embryo model

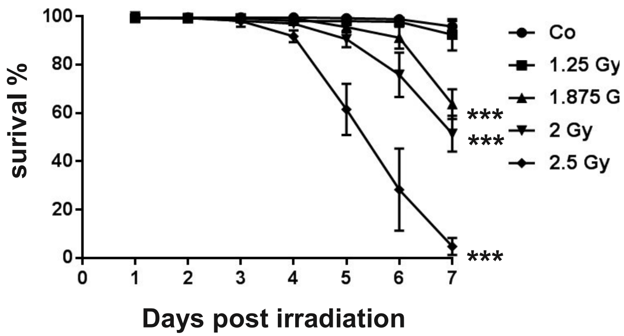
Photon (6 MV)



Fission neutron (<En=1 MeV>)

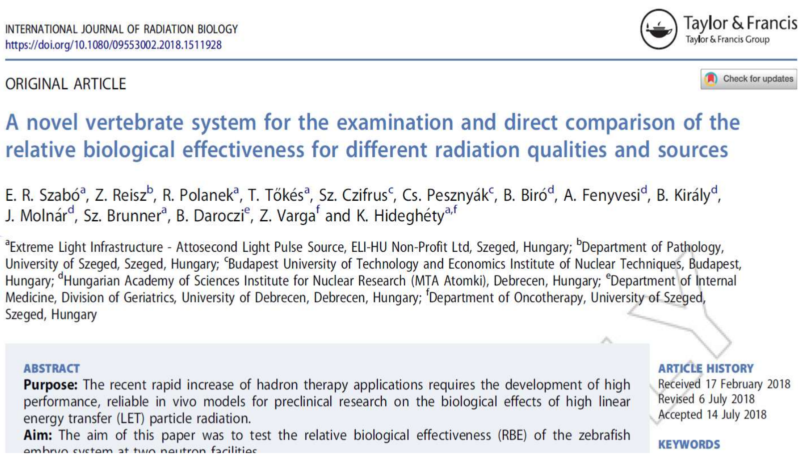


Cyclotron neutron (p(18 MeV)+Be,<En>=3.5 MeV)



$RBE_{Fission}=LD_{50}f/LD_{50}n=20/2=10$

$RBE_{cyclotron}=LD_{50}f/LD_{50}n=20/8=2.5$



INTERNATIONAL JOURNAL OF RADIATION BIOLOGY
https://doi.org/10.1080/09553002.2018.1511928

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ORIGINAL ARTICLE

A novel vertebrate system for the examination and direct comparison of the relative biological effectiveness for different radiation qualities and sources

E. R. Szabó[a], Z. Reisz[b], R. Polanek[a], T. Tőkés[a], Sz. Czifrus[c], Cs. Pesznyák[c], B. Biró[d], A. Fenyvesi[d], B. Király[d], J. Molnár[d], Sz. Brunner[a], B. Daroczi[e], Z. Varga[f] and K. Hideghéty[a,f]

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ABSTRACT

Purpose: The recent rapid increase of hadron therapy applications requires the development of high performance, reliable in vivo models for preclinical research on the biological effects of high linear energy transfer (LET) particle radiation.

Aim: The aim of this paper was to test the relative biological effectiveness (RBE) of the zebrafish embryo system at two neutron facilities

ARTICLE HISTORY
Received 17 February 2018
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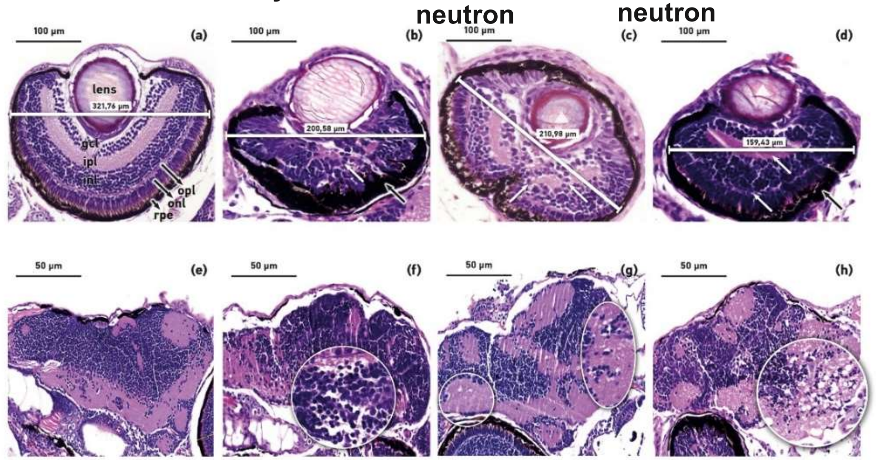
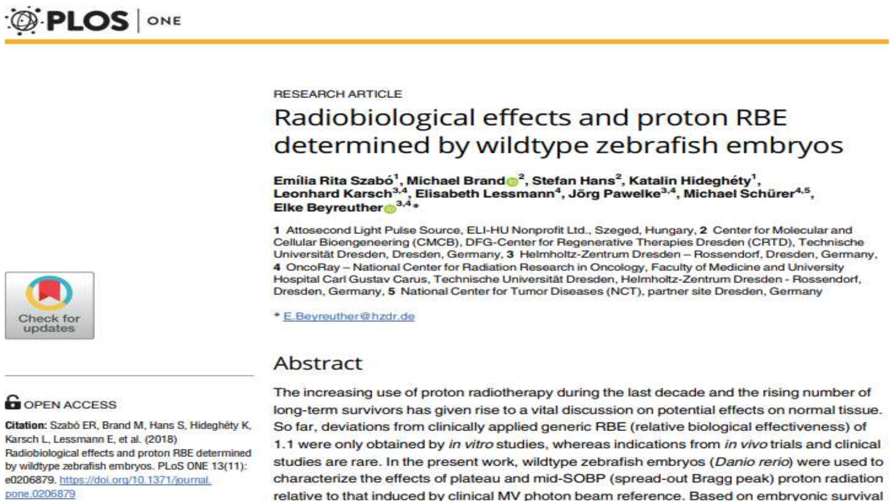
KEYWORDS

Control | **20 Gy - Photon** | **2 Gy – Fission neutron** | **8.12 Gy - Cyclotron neutron**



Previous and ongoing projects

Collaboration with HZDR and OncoRay Dresden: proton irradiation, DRACO-proton irrad, FLASH experiments


PLOS | ONE

RESEARCH ARTICLE

Radiobiological effects and proton RBE determined by wildtype zebrafish embryos

Emília Rita Szabó[1], Michael Brand[2], Stefan Hans[2], Katalin Hideghéty[1], Leonhard Karsch[3,4], Elisabeth Lessmann[4], Jörg Pawelke[3,4], Michael Schürer[4,5], Elke Beyreuther[3,4]*

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* E.Beyreuther@hzdr.de

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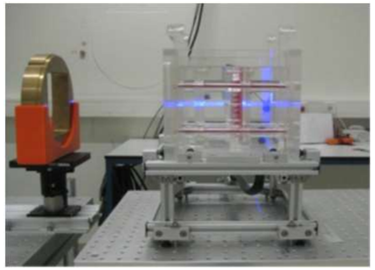
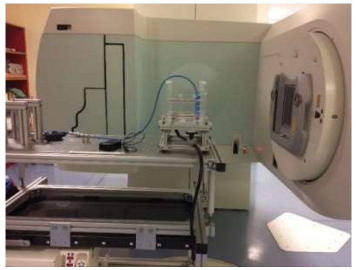
OPEN ACCESS

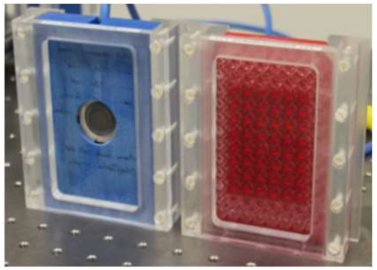
Citation: Szabó ER, Brand M, Hans S, Hideghéty K, Karsch L, Lessmann E, et al. (2018) Radiobiological effects and proton RBE determined by wildtype zebrafish embryos. PLoS ONE 13(11): e0206879. https://doi.org/10.1371/journal.pone.0206879

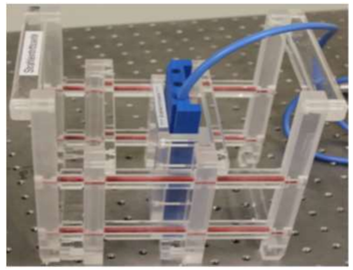
Abstract

The increasing use of proton radiotherapy during the last decade and the rising number of long-term survivors has given rise to a vital discussion on potential effects on normal tissue. So far, deviations from clinically applied generic RBE (relative biological effectiveness) of 1.1 were only obtained by *in vitro* studies, whereas indications from *in vivo* trials and clinical studies are rare. In the present work, wildtype zebrafish embryos (*Danio rerio*) were used to characterize the effects of plateau and mid-SOBP (spread-out Bragg peak) proton radiation relative to that induced by clinical MV photon beam reference. Based on embryonic survival

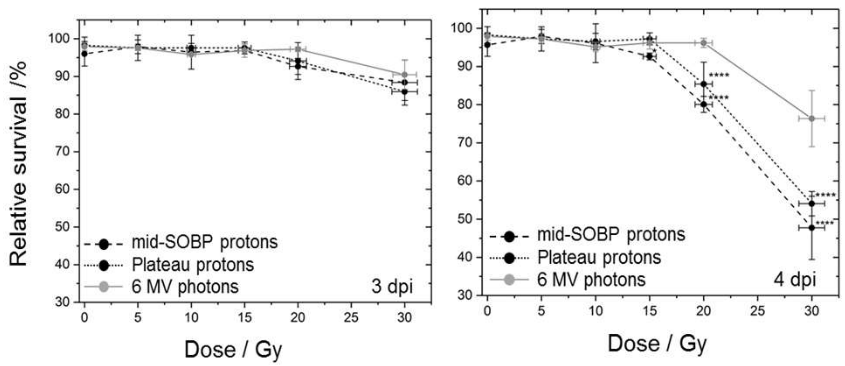








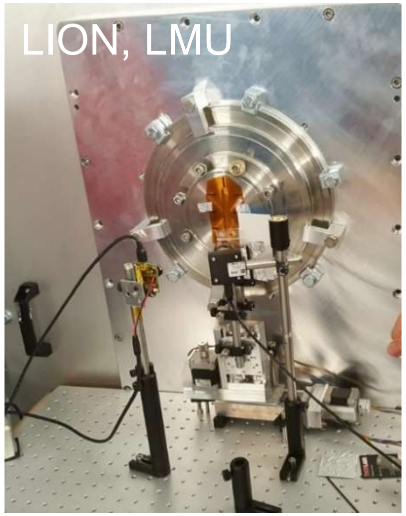
	mid-SOBP	plateau
RBE_{30Gy} ± se	1.60 ± 0.32	1.41 ± 0.08
RBE_{20Gy} ± se	1.20 ± 0.04	1.13 ± 0.08

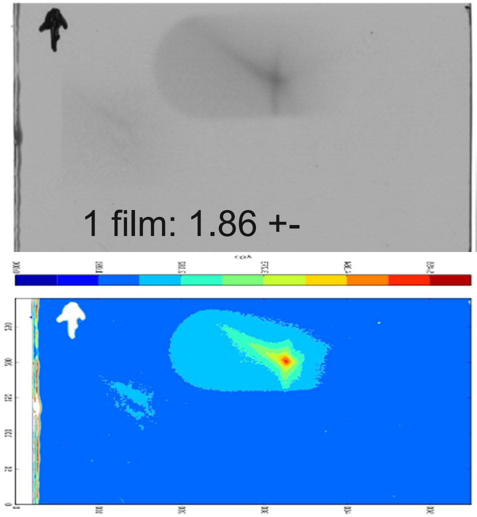


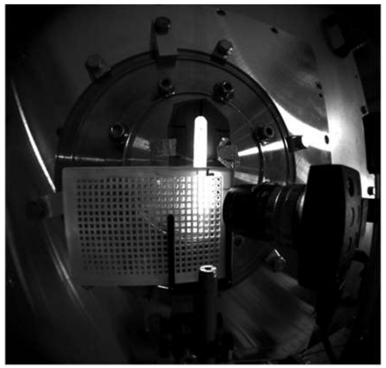
Previous and ongoing projects

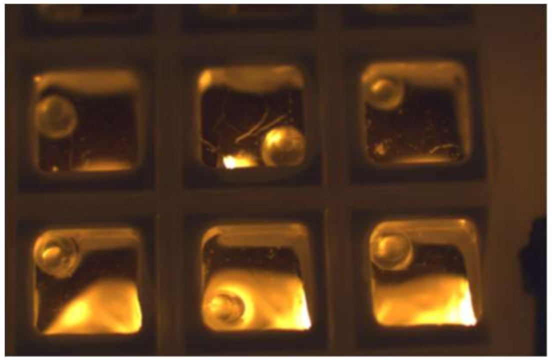
In vivo experiment at laser driven proton facility

Thomas F. Rösch, Zoltán Szabó, Daniel Haffa, Jianhui Bin, Szilvia Brunner, Franz S. Englbrecht, Anna A. Friedl, Ying Gao, Jens Hartmann, Peter Hilz, Christian Kreuzer, Florian H. Lindner, Tobias M. Ostermayr, Róbert Polanek, Martin Speicher, Emília R. Szabó, Derya Taray, Tünde Tőkés, Matthias Würl, Katia Parodi, Katalin Hideghéty and Jörg Schreiber **A feasibility study of Zebrafish embryo irradiation with laser accelerated protons** – Scientific Reports - submitted





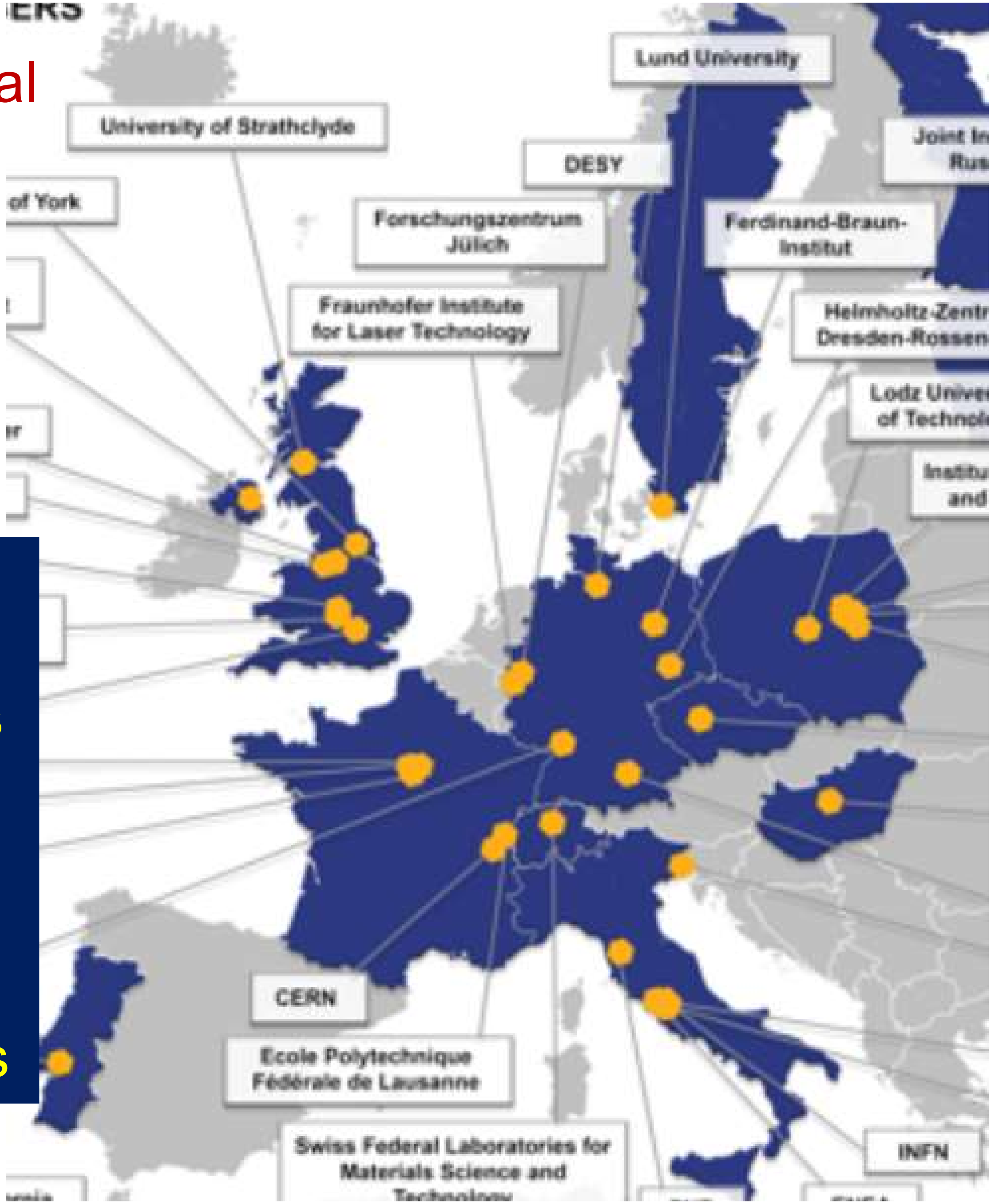




The proton spot size can be reduced to micrometre dimensions without significant loss of particle numbers. Together with the short bunch duration of the order of nanoseconds and below, this would enable very high peak dose rates and highly localized irradiation in microscopic areas.

ZF model provides reliable quantitative biological endpoints (macro- and micro-morphological changes molecular processes).

Integradted Radiobiological Research (IRR) within EUPRAXIA



ZF embryo model can be used, as part of IRR at different centers for cross comparison of biological effects of plasma accelerated ionizing radiation beams in operation at different sites

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University of Szeged

National Laser-initiated Transmutation Laboratory

(laboratories at Dept Optics and in ELI-ALPS)

Karoly Osvay

National Laser-Initiated Transmutation Laboratory University of Szeged

LASER DEVELOPMENTS

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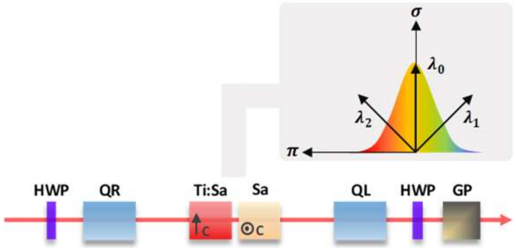
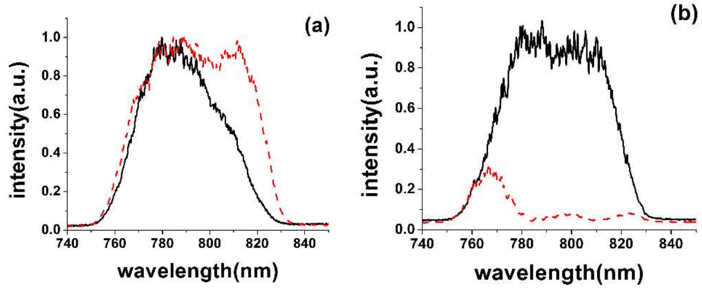
Exploring new amplification schemes

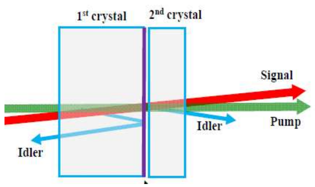
Polarization-encoded chirped pulse amplification in Ti:S

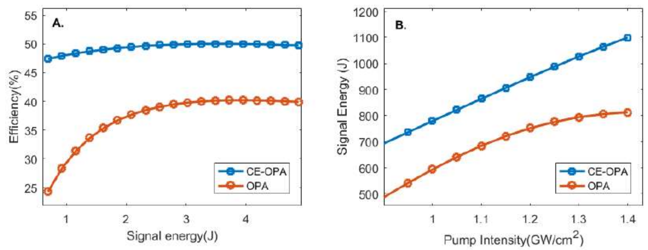




Cao et al, Las. Phys. Lett. 15, 045003 (2018)

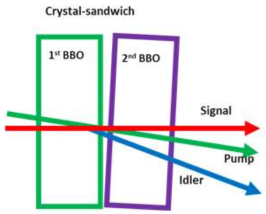
Highly efficient, cascaded extraction optical parametric amplifier

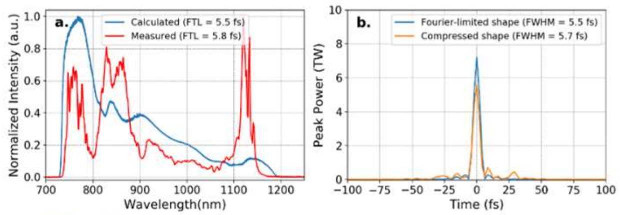




Cao et al., Optics Express 26, 7516 (2018)

Efficient amplification of energetic sub-6fs via OPCPA





Sz. Toth et al., JOSA B 36, 3539 (2019)

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LASER DEVELOPMENTS

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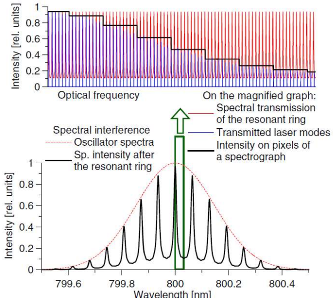
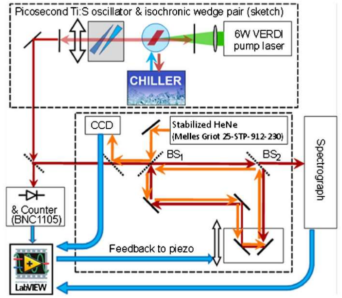
Development of diagnostics

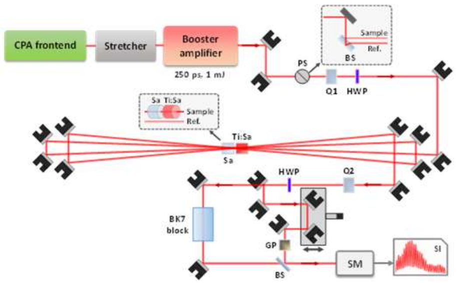
CEP drif measurement of ps pulses

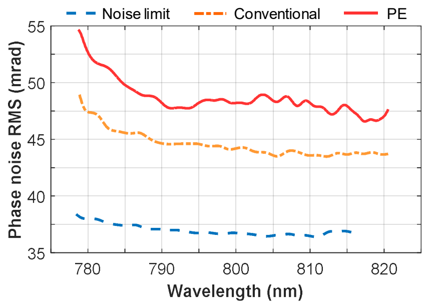




Jojart et al, Opt.Lett. 39, 5914 (2014)

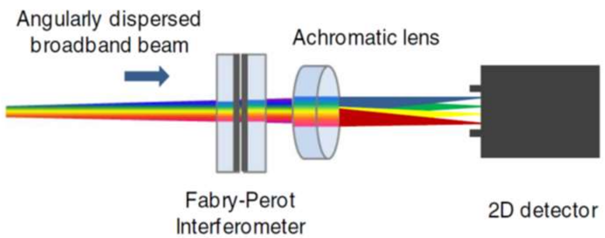
CEP noise measurement upon PE-CPA





Nagymihaly et al, JOSAB **35** (2018) A1

Single-shot measurement of angular dispersion



Börzsönyi et al, OL **38,** 410 (2013)

LASER DEVELOPMENTS

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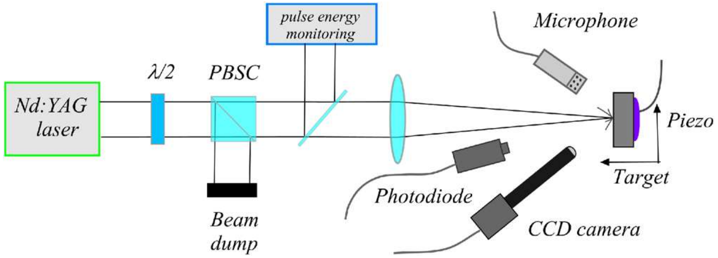
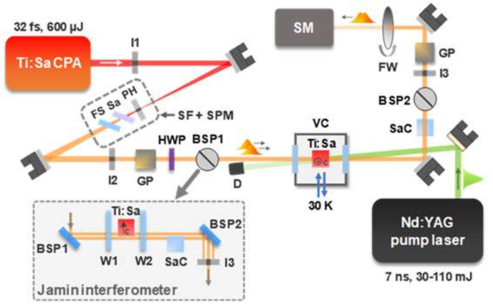
Testing optical components

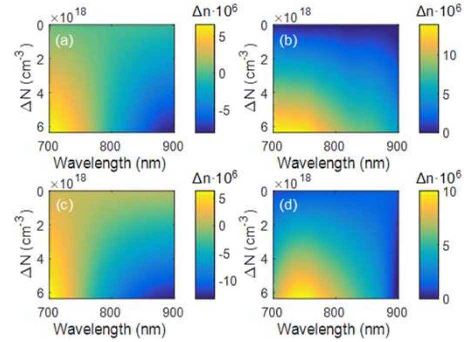
Towards on-line damage monitoring



Somoskői et al., Laser Phys. 25, 056002 (2015)
Somoskői et al., Laser Phys. 30, 046002 (2020)

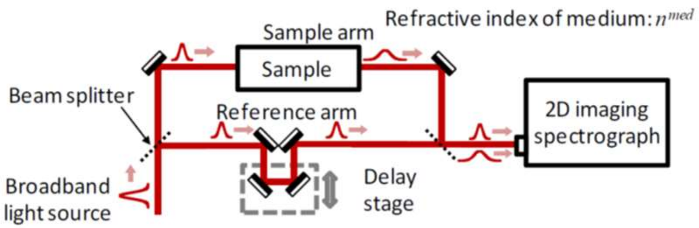
Gain induced phase changes in ti:sapphire





Nagymihaly et al, Opt. Expr. **27** (2019) 1226

Linear and nonlinear dispersion measurements



Borzsonyi et al, Appl.Sci. 3, 515 (2013) - reiew

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Laser development in the TeWaTi lab current system

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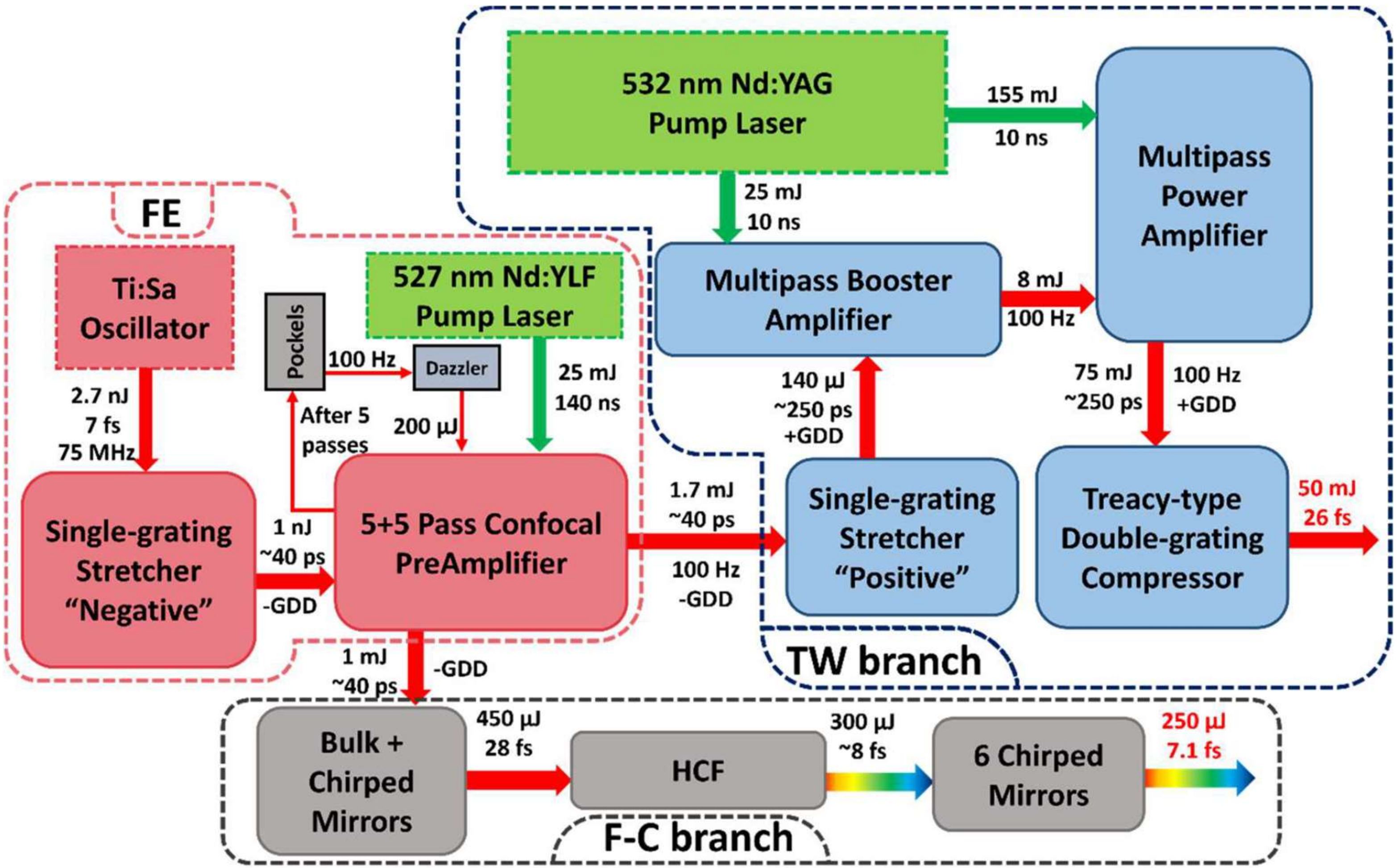

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Laser development in the TeWaTi lab

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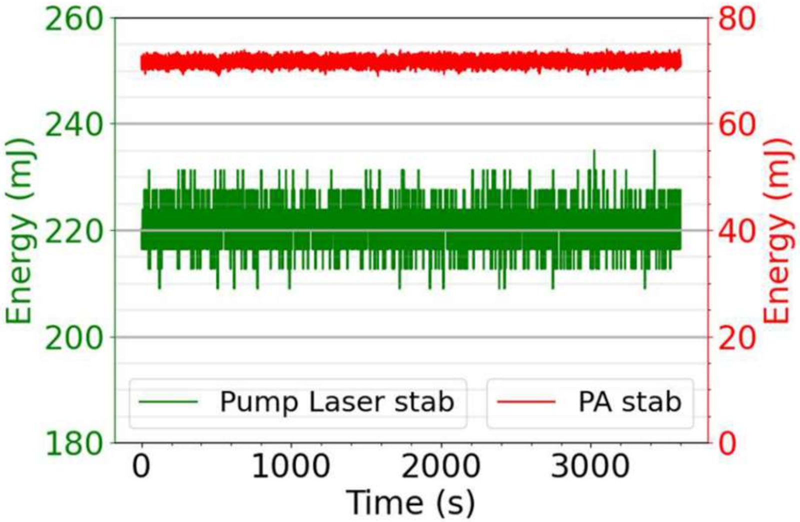
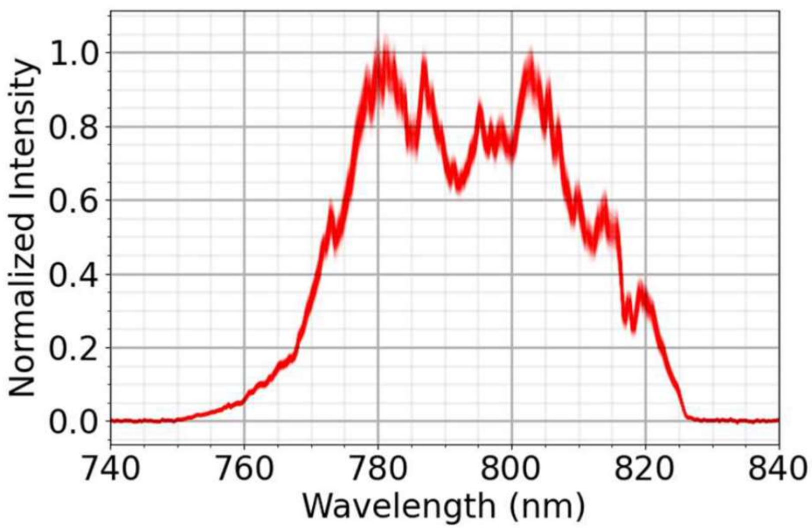
In cooperation with the Cooperative Technologies National Laboratory

High stability, long term operation

Energy: 0.84 %



Pulse duration: <1%



Gaal et al, Appl.Sci. (2024) submitted

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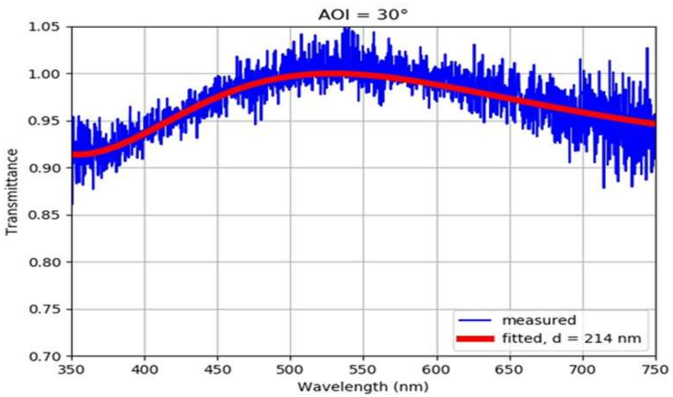
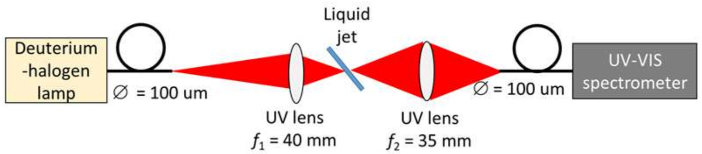
Development of a 200nm thin liquid leaf target system

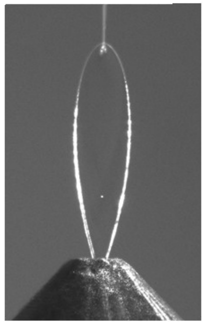
HUNGARIAN NATIONAL LABORATORY

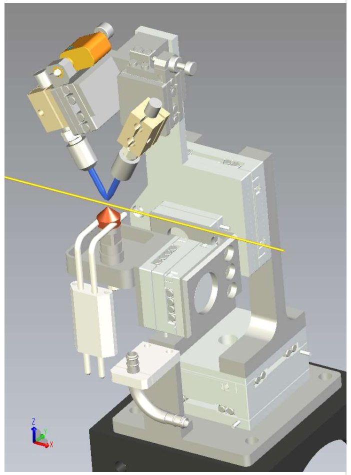
Advanced Microfluidic Systems GmbH

Thickness measurement (in air and in vacuum)

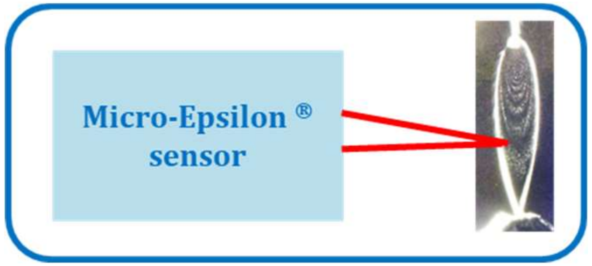


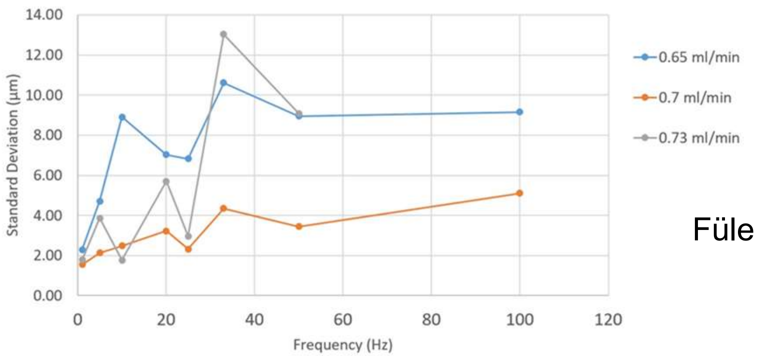






Mechanical stability / resonance measurement





Füle et al, HPLSE **12** (2024) e37

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State of the art neutron generation at 10 Hz repetition rate (~6 hours)

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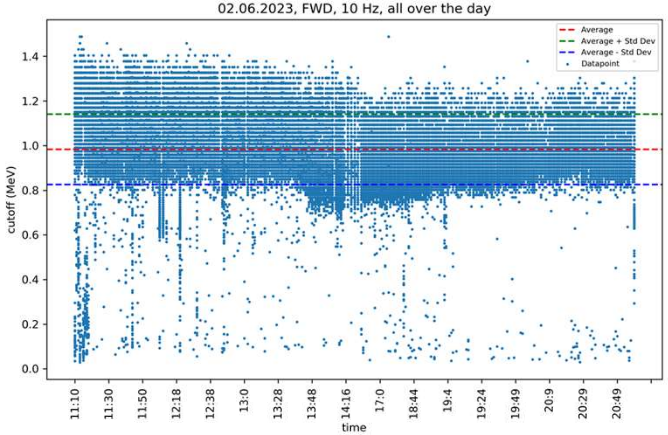
cut-off for the day: 0.98±0.16 (MeV)

Deuteron acceleration from liquid

- at 10 Hz, SEA laser
- at *230mW (80mW)* average power
- 200nm D_2O leaf + 0.1mm C_2D_4

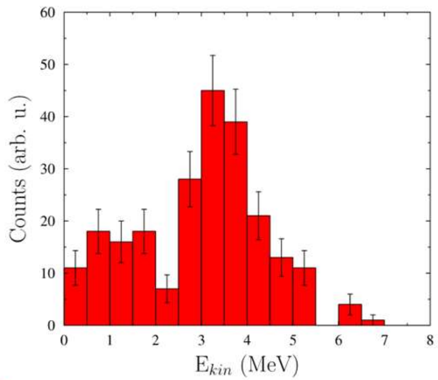


Osvay et al, EPJ Plus **139** (2024) 574

Neutron generation

- 200nm D_2O leaf + 0.1mm C_2D_4
- fusion neutron spectra peaks ~3 MeV

~1.5×10^5 n/s



Peak yield detected 2023/24 at 1kHz : **~10^8 n/s**

- at *100W (20W)* average power

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First radiobiology experiment with laser-generated neutrons

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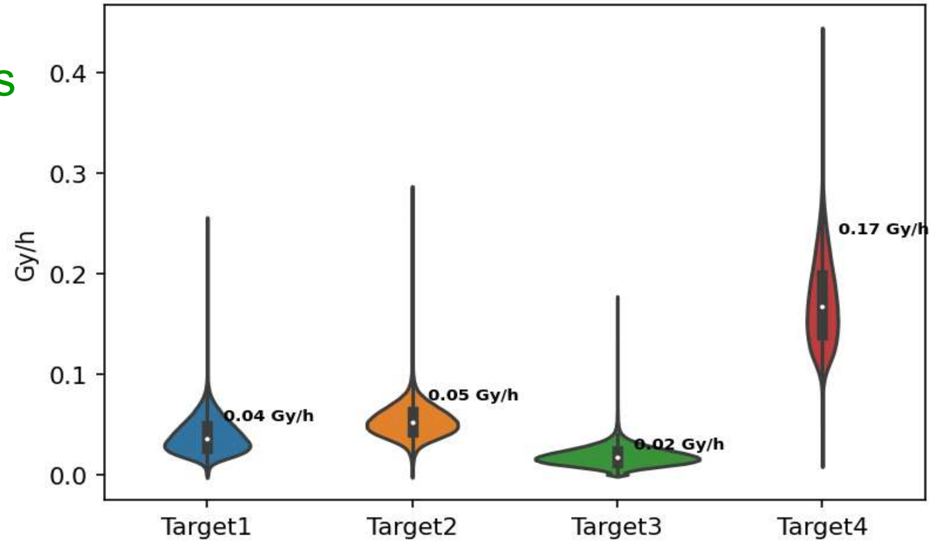
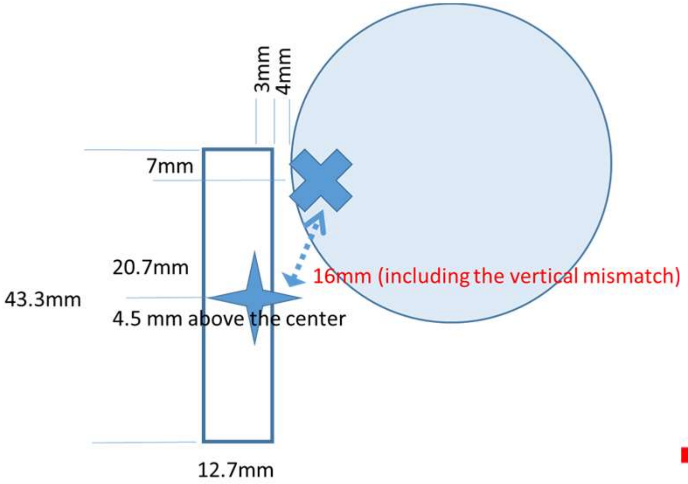
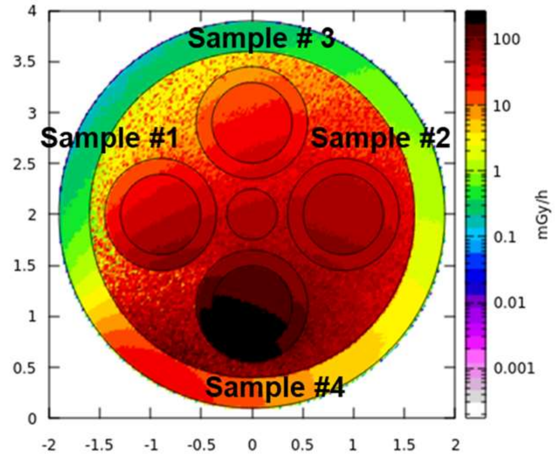
MC-calculated neutron dose on the samples

Largest delivered dose (#4) : **0.27Gy**







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First radiobiology experiment with laser-generated neutrons

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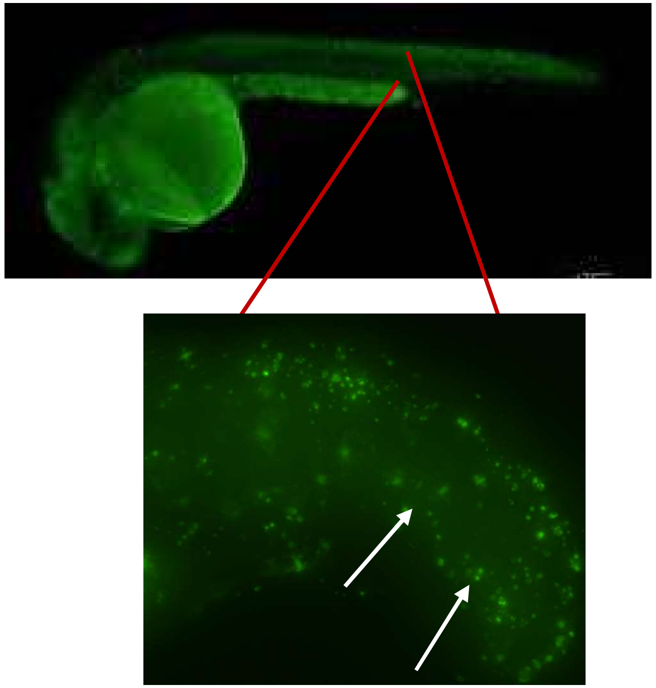
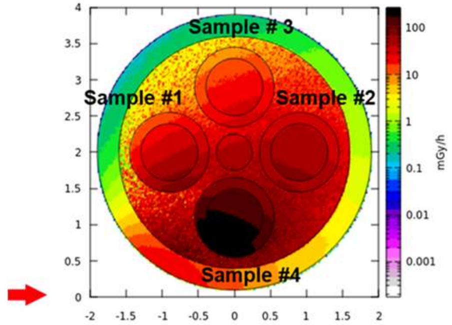
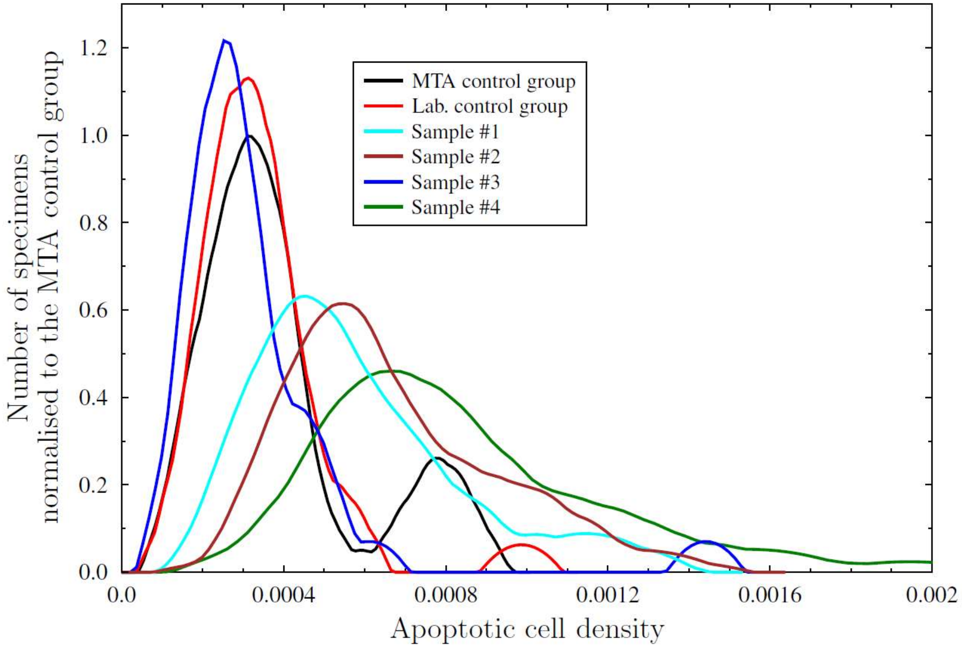
Apptotic cell density







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