

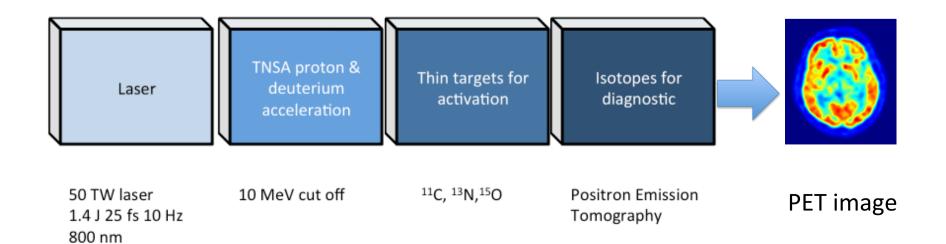
#### Outline

- Motivation
- Initial question
- How to estimate the prospects for PET.
- · Simulations on ion acceleration in nano structured targets
- Conclusions

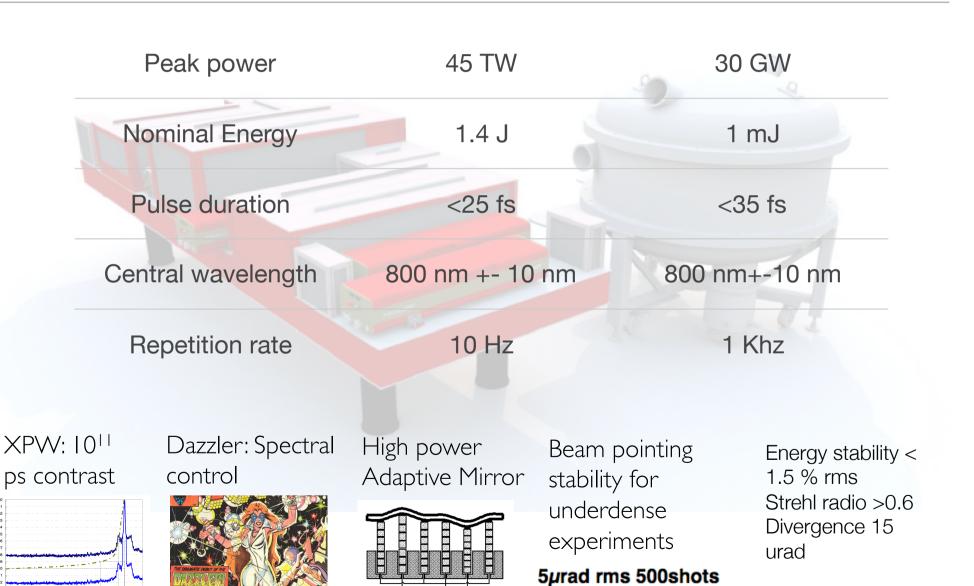
# L2A2: Laser Laboratory for Acceleration and Applications at the USC

#### Objectives:

- Establish the new lab
- · Do basic science in laser plasma acceleration
- Try to push new technology for radioisotope production from laser driven ions.
- One of the important applications of laser driven plasma accelerators is the use of protons to produce radioisotopes.
- The production of short-lived isotopes such as <sup>11</sup>C or <sup>18</sup>F is important in medicine for positron-emission tomography (PET).



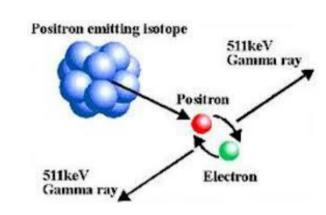
# Laser system @ L2A2



# Motivation: Positron Emission Tomography (PET)

PET is considered the most sensitive 3D imaging technique:

- -Positrons emitted by specific  $\beta^+$  radionuclides annihilate producing two photons
- -The back-to-back emission of pairs of photons from a given volume made it possible its reconstruction using appropriate image reconstruction algorithms



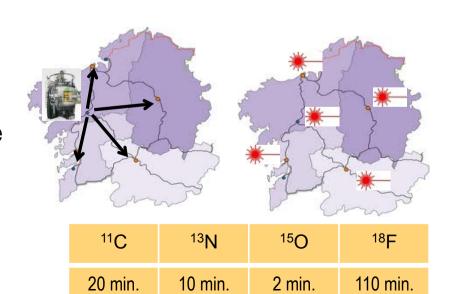
The production of radionuclides requires an accelerator with a complex infrastructure :

- -The production strategy is based on a regional production center and distribution.
- -Short-lived emitters can only be used close to the production center

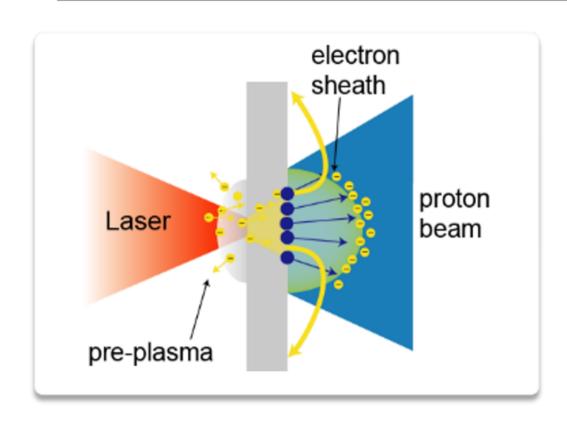
#### Laser accelerators may represent an option:

Simpler and cheaper infrastructure.

Compact device that could be installed in any hospital for the production of short-lived radioisotopes



# Target Normal Sheath Acceleration (TNSA)



#### Characteristics

- Broad spectra
- High number of protons:  $10^{10}$ - $10^{13}$
- Low emittance: 4x10<sup>-3</sup> mm/mrad
- Divergence 10-20 degrees
- Ultrashort 0.1-10 ps

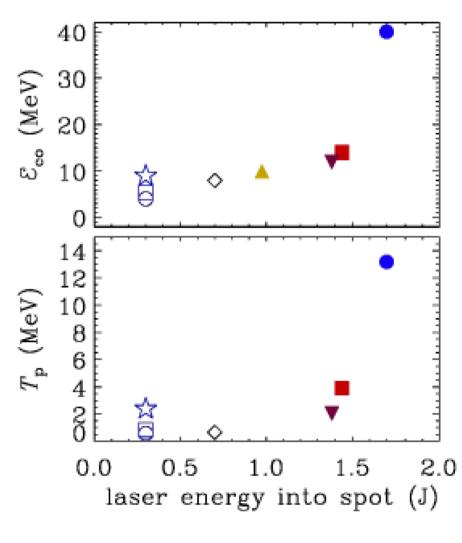
Snavely et al, PRL **85** (2000) 2945 Other observations: Clark et al, PRL **84** (2000) 670 Maksimchuk et al, PRL **84** (2000) 4108

Ion acceleration by superintense laser-plasma interaction Andrea Macchi, Marco Borghesi, and Matteo Passoni Rev. Mod. Phys. 85, 751

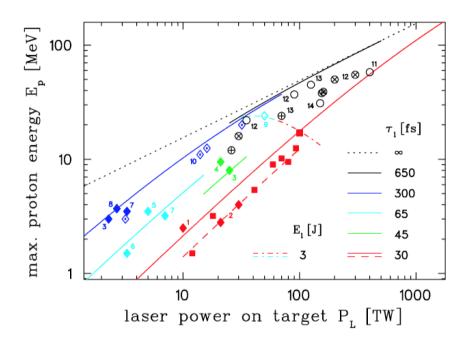
# Why TNSA?

- The most studied phenomena
- Achievable with <2J per pulse</li>
- Micron thick targets instead of nm thick targets
- Several routes for optimization described
- A broad spectrum is useful depending on the cross section
- progress should be monitored on small-scale lasers with potential for high repetition rate and cost-effective applications
  A. Macchi

# TNSA Protons: Laser energy below 2J



A. Macchi



K Zeil, et al, NJP 12 (2010) 045015 (16pp)

- · Overdense.
- TNSA
- 10 um Al foils
- Single shot
- 10 MeV protons

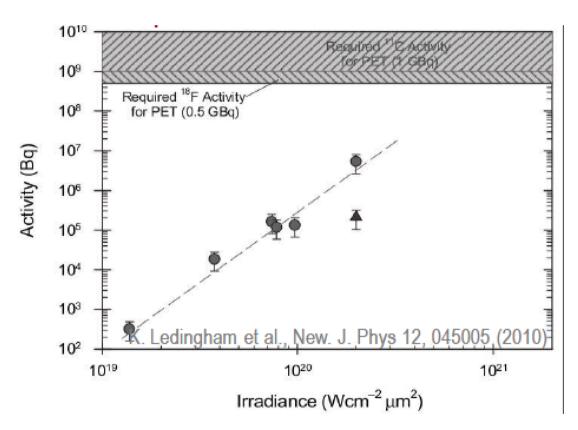
# Initial question.

 Would it be possible to produce radioisotopes for medical imaging such as PET from laser driven ions?

# The initial question: Activation by laser produced protons

120 J, ~1 ps (10<sup>20</sup> W/cm<sup>2</sup>), CR ~10<sup>6</sup>
 11C activity/shot ~ 200 kBq
 I. Spencer et al., NIMB 183, 449 (2001)

- 20-30 J, 0.3 0.8 ps (1-6 10<sup>19</sup> W/cm<sup>2</sup>), CR <10<sup>6</sup> <sup>11</sup>C activity/shot ~ 1 MBq J. Fuchs et al., PRL 94, 045004 (2005)
- 0.8 J, 40 fs (6 10<sup>19</sup> W/cm<sup>2</sup>), CR <10<sup>6</sup>
   11C activity/shot ~ 1.2 kBq
   S. Fritzler et al., App. Phys. Lett. 83, 3039 (2003)



I. Spencer, et al, Nuclear Instruments and Methods in Physics Research Section B: Beam Interactions with Materials and Atoms 183 (2001) 449.

S. Fritzler, et al, Appl. Phys. Lett. 83 (2003) 3039.

K. W. D. Ledingham, et al, J. Phys. D: Appl. Phys. 37 (2004) 2341.

L. Robson, et al, High-power laser production of pet isotopes, Lecture Note in Physics 694 (2006) 191.

#### One estimation from 2006

JOURNAL OF APPLIED PHYSICS 100, 113308 (2006)

# Numerical simulation of isotope production for positron emission tomography with laser-accelerated ions

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Sven Fritzler

Siemens Medical Solutions, Vacuum Technology, 91052 Erlangen, Germany

Victor Malka

Laboratoire d'Optique Appliquée, ENSTA, UMR 7639 CNRS/Ecole Polytechnique, 91761 Palaiseau, France

$$I = 10^{20} W/cm^2$$

$$^{11}C$$
  $1.1 \times 10^8$  per shot

$$^{18}F$$
  $3.1 \times 10^{7}$  per shot 9.7 Gbq 1Khz 1hr

$$I = 4 \times 10^{20} W/cm^2$$

### New estimation 2016

Study of the production yields of <sup>18</sup>F, <sup>11</sup>C, <sup>13</sup>N and <sup>15</sup>O positron emitters from plasma-laser proton sources at ELI-Beamlines for labeling of PET radiopharmaceuticals

Ernesto Amato <sup>a</sup>, Antonio Italiano <sup>b,\*</sup>, Daniele Margarone <sup>c</sup>, Benedetta Pagano <sup>d</sup>, Sergio Baldari <sup>a,d</sup>, Georg Korn <sup>c</sup>

Table 2

Total radionuclide activities produced at the end of bombardment (EOB), for different laser repetition rates and irradiation times, for the three proton spectra, according to Table 1.

Nuclide	T <sub>1/2</sub> (min)	A <sup>CYCL</sup> (MBq)	T <sub>irr</sub> <sup>CYCL</sup> (min)	Rep. rate (Hz)	1			5			10		
				T <sub>irr</sub> (min)	15	60	120	15	60	120	15	60	120
<sup>18</sup> F	110	52000 (F <sup>-</sup> )	60	spectrum	Total Activity at EOB (MBq)								
				low	1.8	6.4	10.8	9.1	31.9	53.8	18.3	63.8	107.5
				medium	11.4	39.6	66.8	56.8	198.2	333.9	113.5	396.3	667.8
				high	54.4	189.8	319.9	271.9	949.2	1599.6	543.9	1898.4	3199.1
11C	20	36000 (CO)	50	spectrum	Total A	Total Activity at EOB (MBq)							
				low	2.0	4.4	5.0	10.2	22.1	24.8	20.4	44.1	49.6
				medium	32.1	69.4	78.1	160.7	346.9	390.3	321.4	693.8	780.5
				high	198.6	428.6	482.2	993.0	2143,2	2411,1	1985.9	4286.4	4822.2
13N	10	4000 (NH <sub>3</sub> )	10	spectrum	Total A	Total Activity at EOB (MBq)							
				low	0.1	0.1	0.1	0.4	0.6	0.6	0.7	1.1	1.1
				medium	44.3	67.5	68.6	221.6	337.5	342.8	443.3	675.0	685.5
				high	502.8	765.7	777.7	2514.2	3828.5	3888.3	5028.4	7657.0	7776.6
<sup>15</sup> O	2	74000 (O <sub>2</sub> )	10	spectrum	Total Activity at EOB (MBq)								
				low	5.7	5.7	5.7	28.5	28.7	28.7	57.0	57.3	57.3
				medium	7.5	7.6	7.6	37.5	37.8	37.8	75.1	75.5	75.5
				high	43.3	43.5	43.5	216.3	217.5	217.5	432.6	435.0	435.0

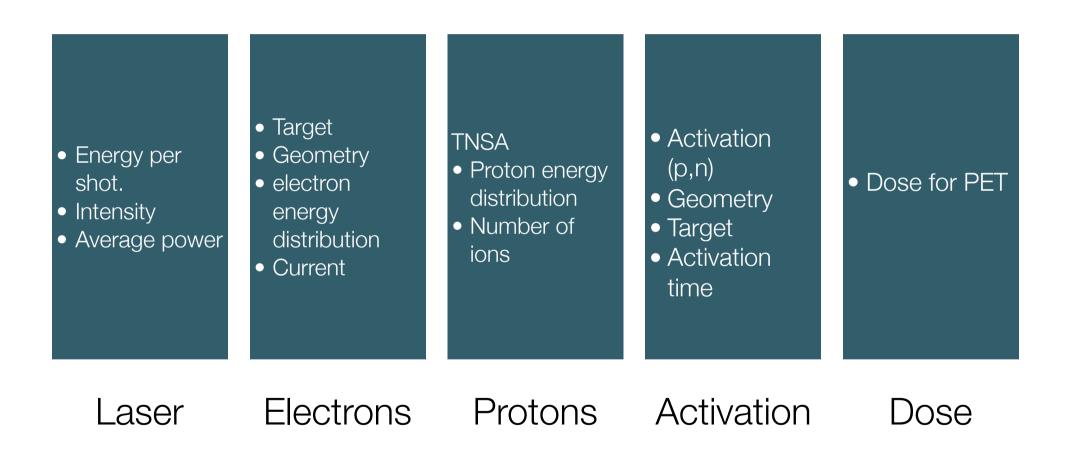
a Section of Radiological Sciences, Department of Biomedical and Dental Sciences and of Morphologic and Functional Imaging, University of Messina, Italy

<sup>&</sup>lt;sup>b</sup> Istituto Nazionale di Fisica Nucleare, Gruppo Collegato di Messina, Italy

<sup>&</sup>lt;sup>c</sup> Institute of Physics ASCR, v.v.i. (FZU), ELI-Beamlines Project, 182 21 Prague, Czech Republic

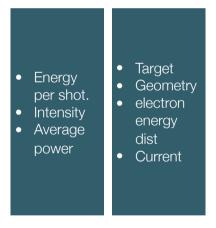
<sup>&</sup>lt;sup>d</sup> Nuclear Medicine Unit, University Hospital "G. Martino", Messina, Italy

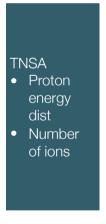
### Diagram of the estimation

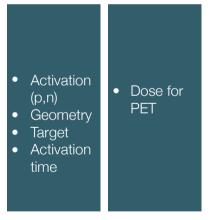


### Diagram of the estimation.

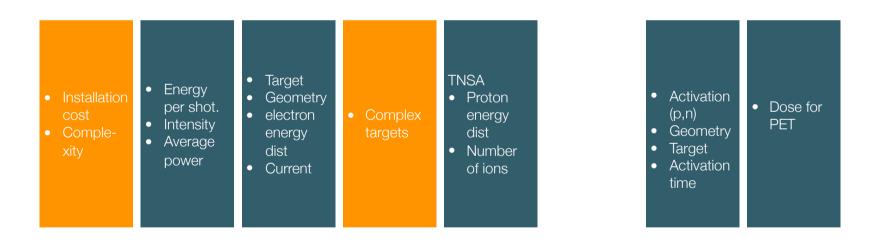
- The estimation compare against the production of a cyclotrons.
- 2006. In order to compete with a regular cyclotron it is necessary to have 1PW, 1Khz.
- 2016. "In principle, the feasibility to produce clinically relevant amounts of positron emitters, to be used for inline preparation of single doses of radiopharmaceuticals,..., peak power (PW) and high repetition rate (10 Hz)".
- Consider a broader perspective.

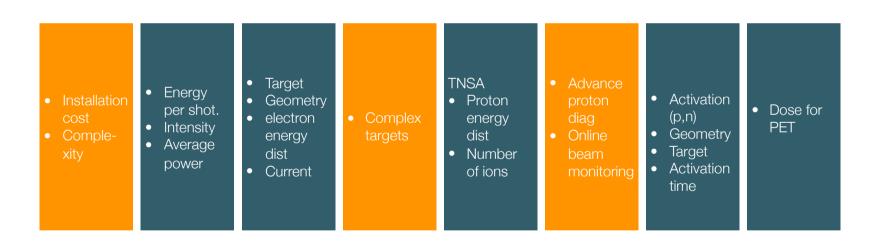


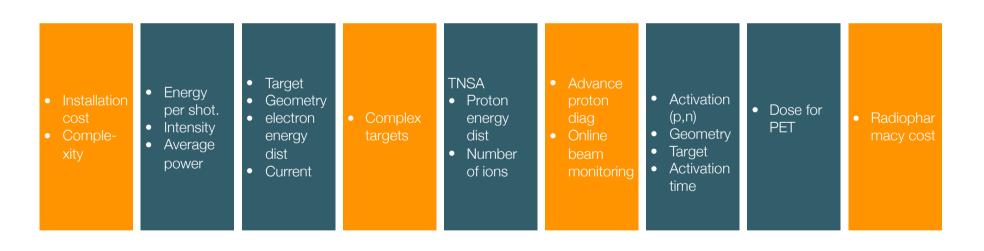


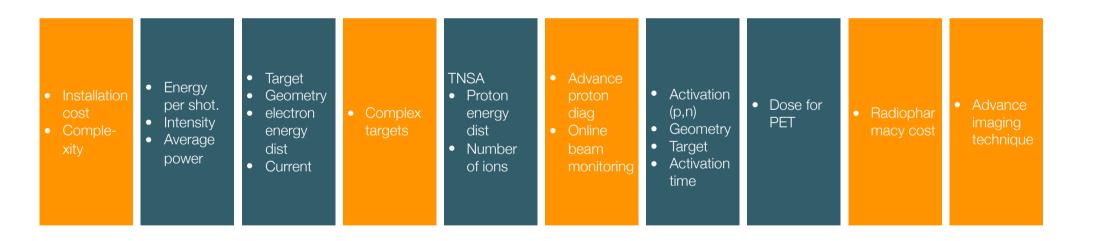




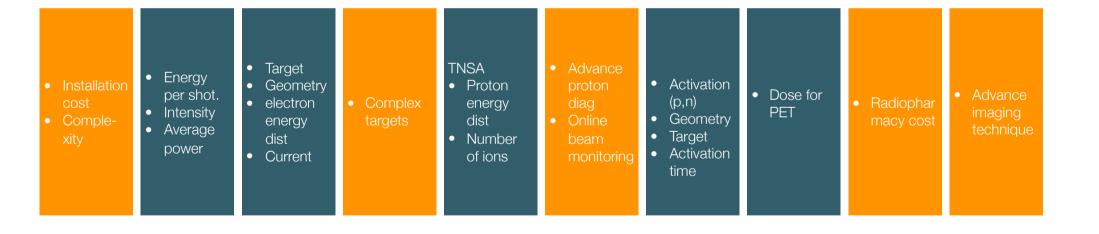








Overall cost & complexity







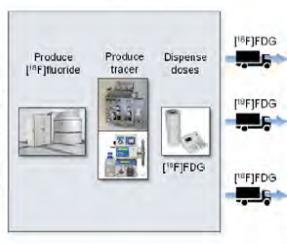
# New paradigm for radio isotope production



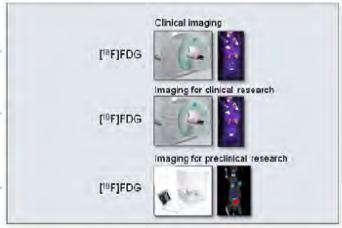
PET Radiopharmacies

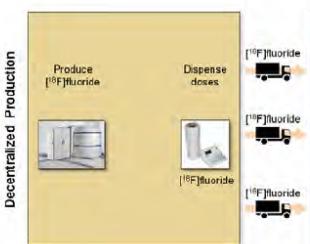


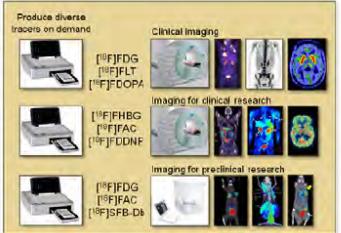
PET Centers



Centralized Production







#### **Emerging Technologies for Decentralized Production of PET Tracers**

Pei Yuin Keng<sup>1</sup>, Melissa Esterby<sup>1,2</sup> and R. Michael van Dam<sup>1</sup> <sup>1</sup>Crump Institute for Molecular Imaging, Department of Molecular & Medical Pharmacology, David Geffen School of Medicine, University of California, Los Angeles

# Overall cost & complexity

- · Large Cyclotrons
- Commercial installations are large facilities
- · A special building
- Designed to produce a large number of doses
- Cost effective use depend on number of PET scanners
- Strong restriction on research related to new pharmaceuticals in preclinical
- Short lifetime (110 min) implies dose will undergo multiple half life of decay before use
- · Careful planning
- · Only FDG

- · Laser
- Not a special building, limited shielding
- Lowest possible energy
- Adjusted to single dose production
- Minimal down time
- Radiopharmacy tuned for single dose (Lab on chip)
- Fully automated extraction

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Only FDG

- Laser
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extraction

# New diagram for the estimation.



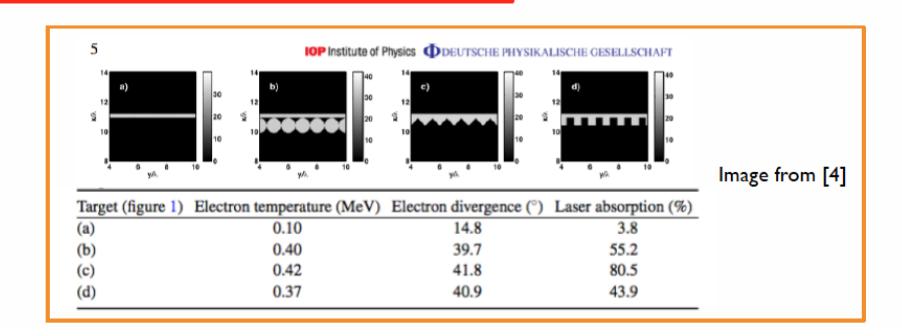
## Nano and micro structured target

#### State of the art

Microstructuring the front of the target surface enhances energy absorption and improves ion acceleration [1-7].

The increased absorption creates more energy available for the particles to be accelerated.

- [1] Phys. Plasmas 18(10) (2011)
- [2] Contrib. Phys. Plasmas 53(2), 173-178 (2013)
- [3] Plasma Phys. and Control. Fusion 58, 014038 (2016)
- [4] New J. Phys. 13, 053028 (2011)
- [5] Phys. Rev. Lett. 109, 234801 (2012)
- [6] Phys. Rev. Lett., 110, 215004 (2013)
- [7] Nature Lett. 439(26), 445-448 (2006)



### Triangular shapes

#### Why a triangular shape?

Proton cutoff and energy absorption are enhanced compared to others [4].

There are prospects of using easier-to-make tilted triangles: possibly better for oblique incidence experiments.

#### **Experimental limitations**

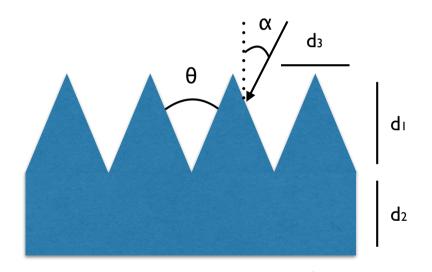
Structure height below a wavelength and below bulk thickness

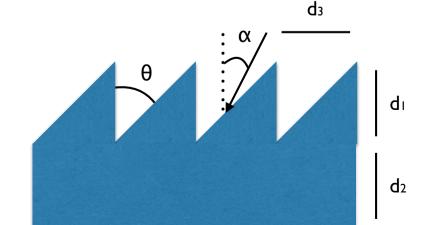
#### Parameters to vary

- The structure height
- The triangle width
- The bulk thickness
- The angle of incidence

#### **Shapes**

The angle of incidence of the laser is represented by  $\alpha$ .





[4] New J. Phys. 13, 053028 (2011)

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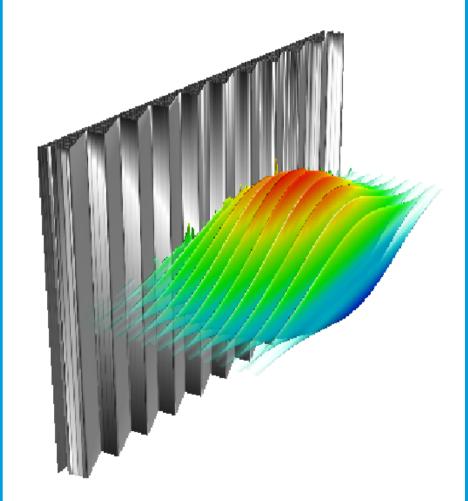
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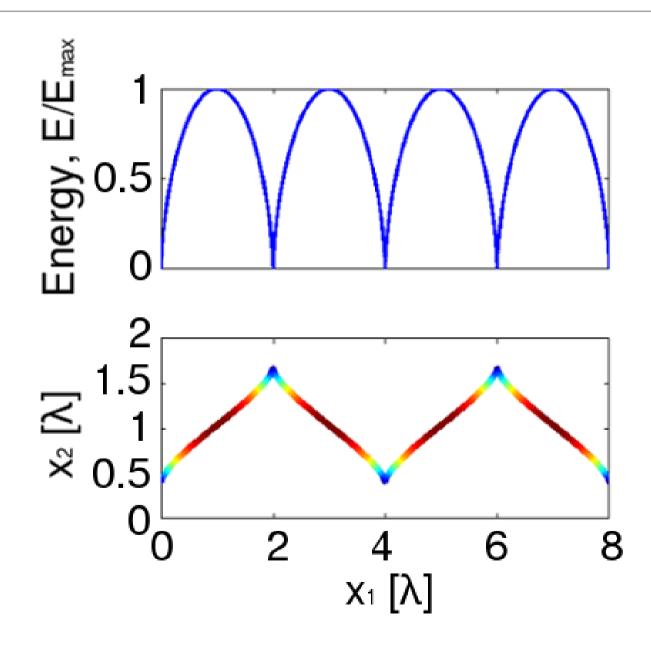
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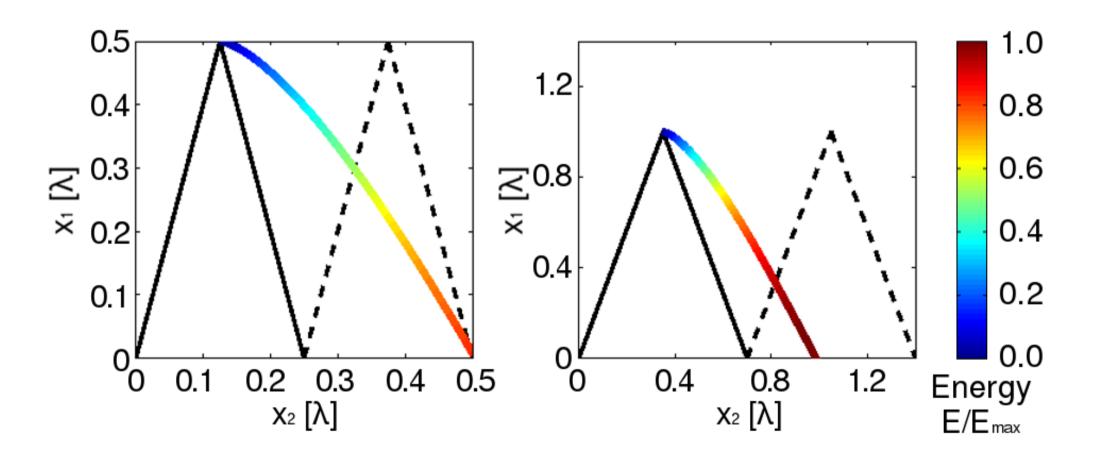
[4] New J. Phys. 13, 053028 (2011)

# Simple idea



### Simple idea

 Use the geometry of the target to optimize the energy delivered by the electron to the target

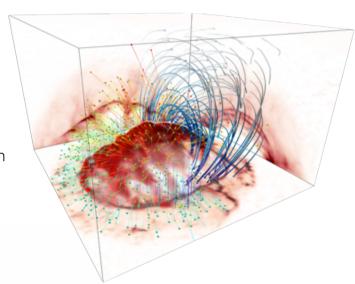


### OSIRIS PIC code



#### osiris framework

- Massivelly Parallel, Fully Relativistic
   Particle-in-Cell (PIC) Code
- Visualization and Data Analysis
   Infrastructure
- · Developed by the osiris.consortium
  - ⇒ UCLA + IST





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#### Frank Tsung

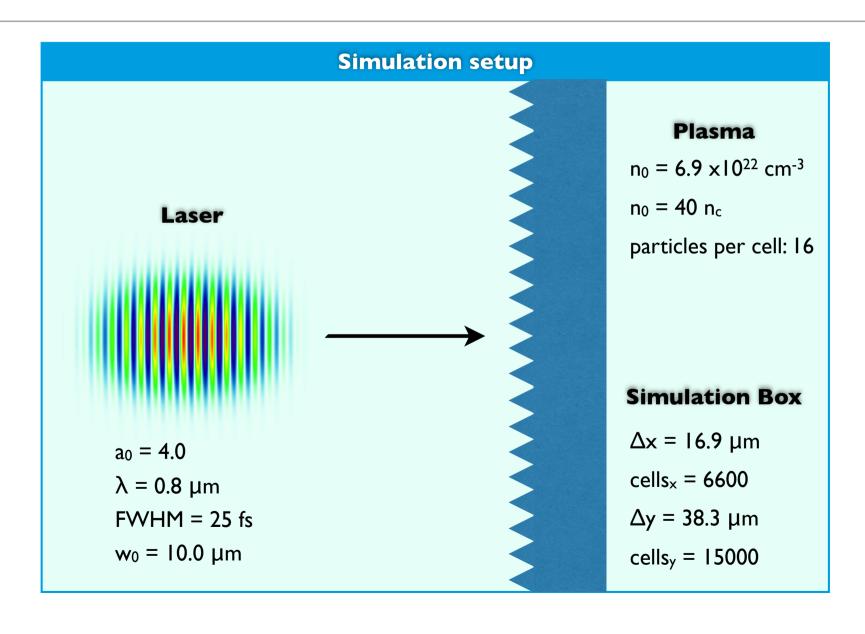
tsung@physics.ucla.edu

http://epp.tecnico.ulisboa.pt/ http://plasmasim.physics.ucla.edu/



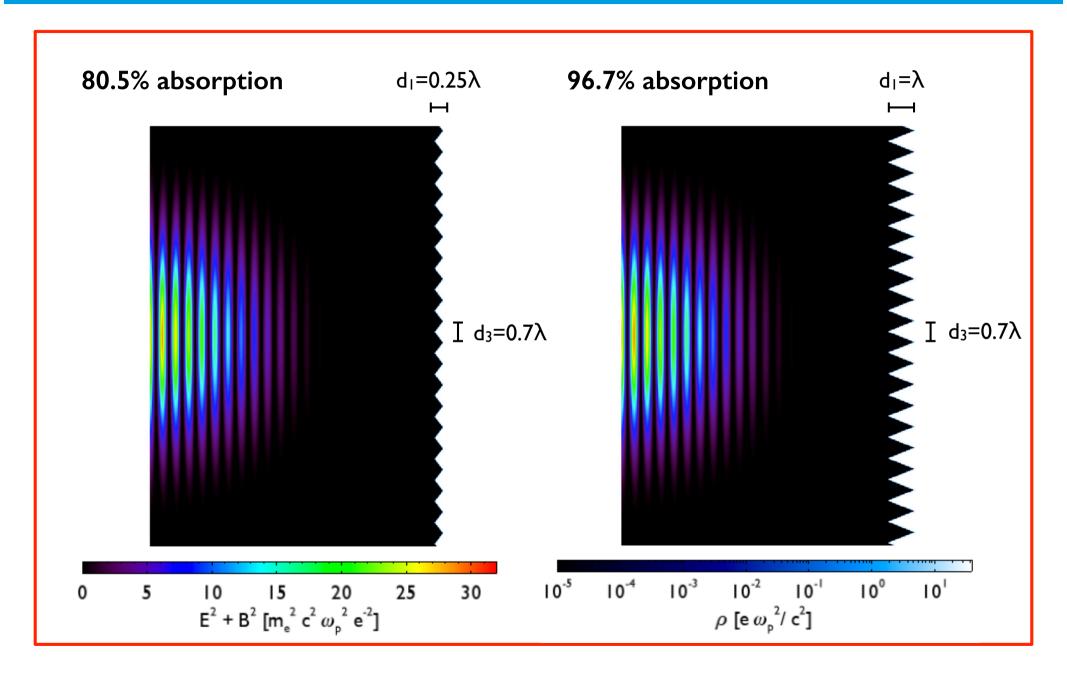
- Scalability to ~ 1.6 M cores
- · SIMD hardware optimized
- · Parallel I/O
- · Dynamic Load Balancing
- · Particle merging
- · GPGPU support
- · Xeon Phi support
- QED Module

# Simulations in 2D for parameter scan



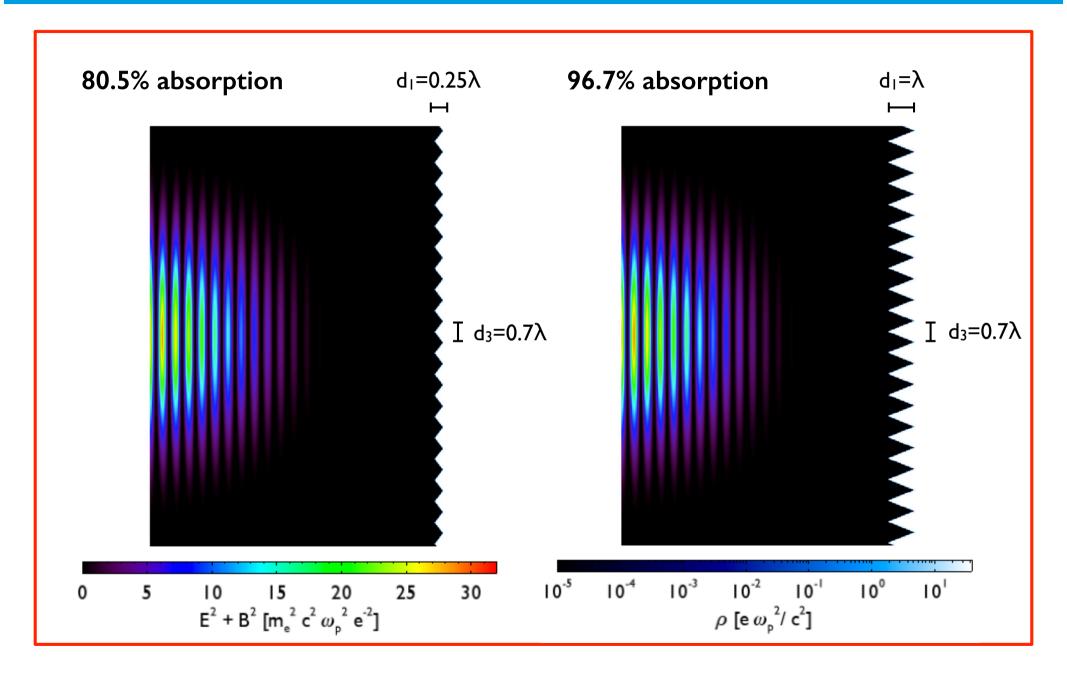
### Different structures mean different absorption





### Different structures mean different absorption



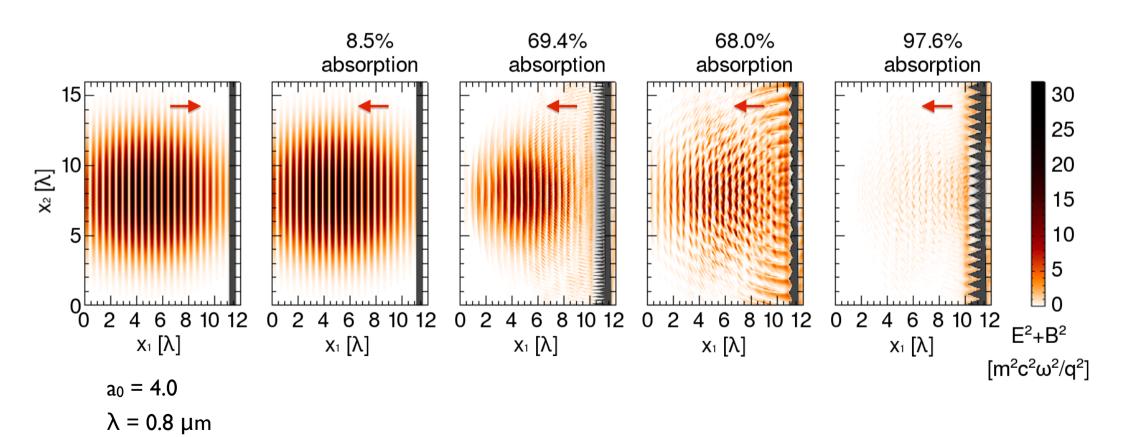


### Laser absorption

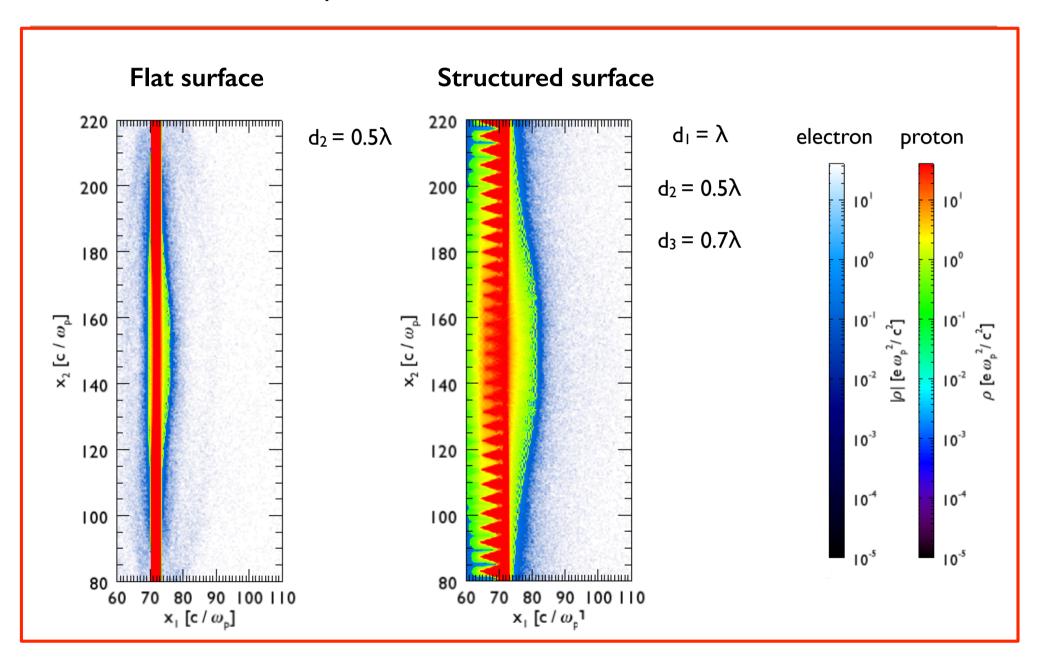
FWHM = 25 fs

 $w_0 = 10.0 \ \mu m$ 

Reflected field for different parameters of the structure



### Mechanism for proton acceleration



### Effect of the width of the triangular structure

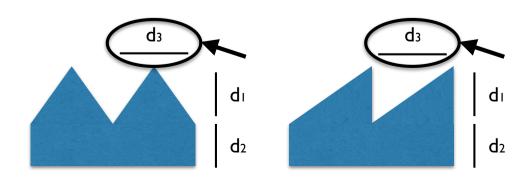
#### Effect of the width

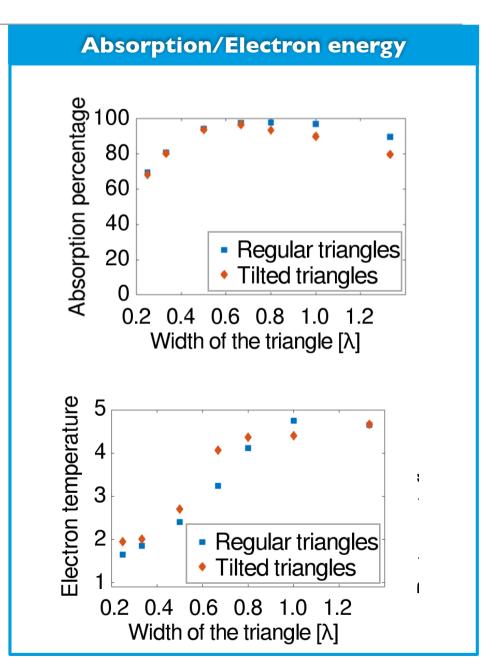
- If  $d_3 << \lambda$ : The structures become invisible.
- If  $d_3 >> \lambda$ : The surface becomes flat.

Model and data show maximum absorption for a width:

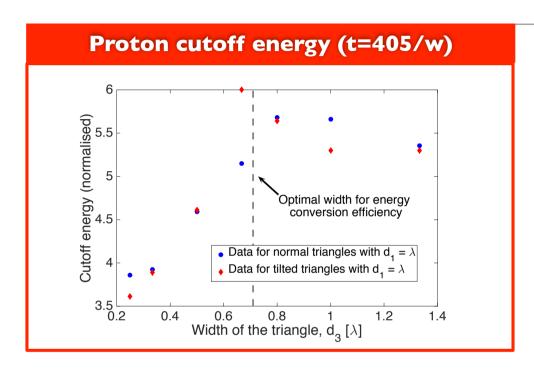
$$d_{3,max} = 2a_0\lambda(\pi n_e)^{-1/2} = 0.7\lambda$$

$$d_2 = 0.5\lambda$$

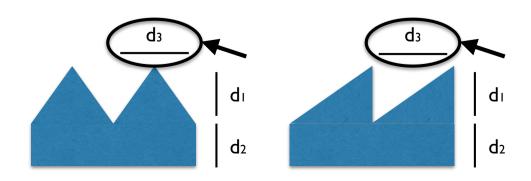


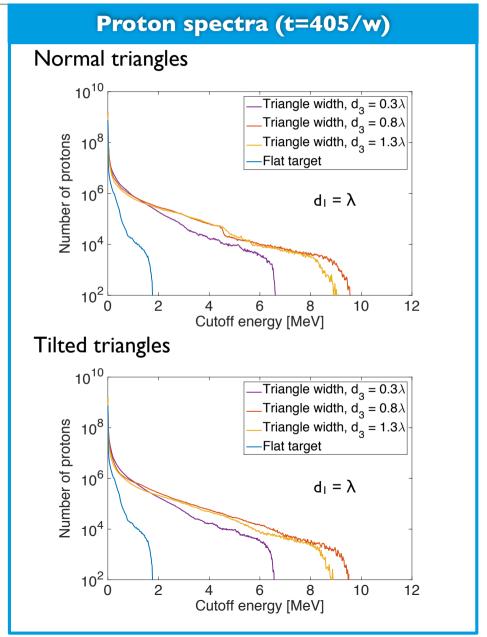


### Effect of the width of the triangular structure



$$d_2 = 0.5\lambda$$

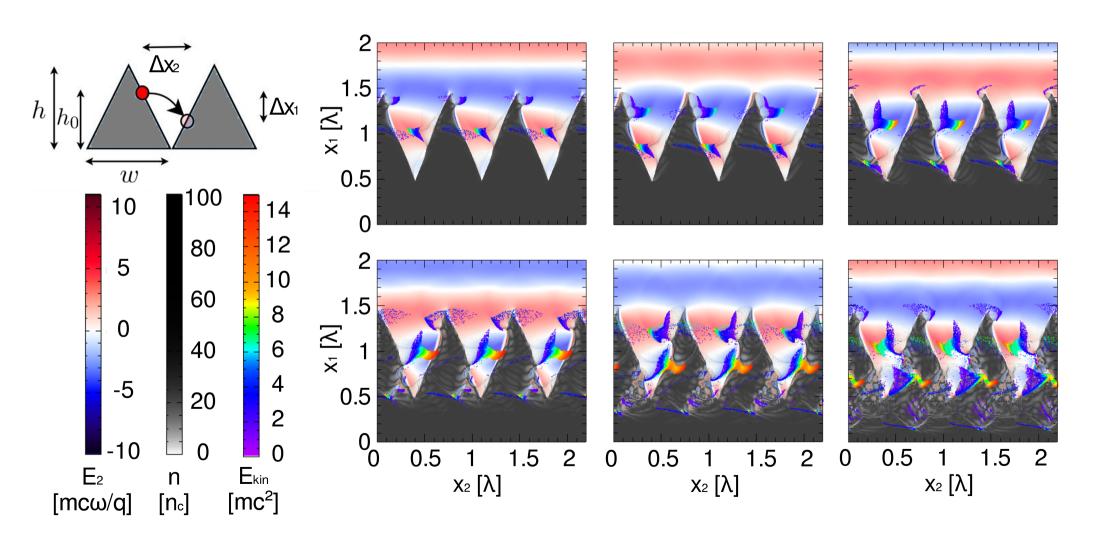




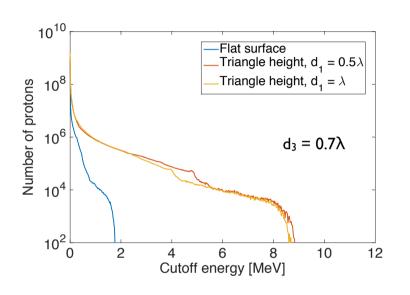
 $\rm E_2$ 0.00 [ 1 /  $\omega_{\rm p}$  ] Time = 10 30 10.00000 5 1.00000 5 25 0.10000 E<sub>2</sub> [m<sub>e</sub> c ω<sub>p</sub> e<sup>-1</sup>]  $|\rho| [e \omega_{\rm p}^2/c^2]$  $x_2 [c/\omega_p]$  $p_2 [m_e c]$ 0 0.01000 20 0.00100 -5 -5 0.00010 15 -10 0.00001  $\begin{array}{cc} 50 & 52 \\ x_1 \ [c \ / \ \omega_p] \end{array}$ 56 46 48 54

 $\rm E_2$ 0.00 [ 1 /  $\omega_{\rm p}$  ] Time = 10 30 10.00000 5 1.00000 5 25 0.10000 E<sub>2</sub> [m<sub>e</sub> c ω<sub>p</sub> e<sup>-1</sup>]  $|\rho| [e \omega_{\rm p}^2/c^2]$  $x_2 [c/\omega_p]$  $p_2 [m_e c]$ 0 0.01000 20 0.00100 -5 -5 0.00010 15 -10 0.00001  $\begin{array}{cc} 50 & 52 \\ x_1 \ [c \ / \ \omega_p] \end{array}$ 56 46 48 54

## Mechanism for efficient absorption

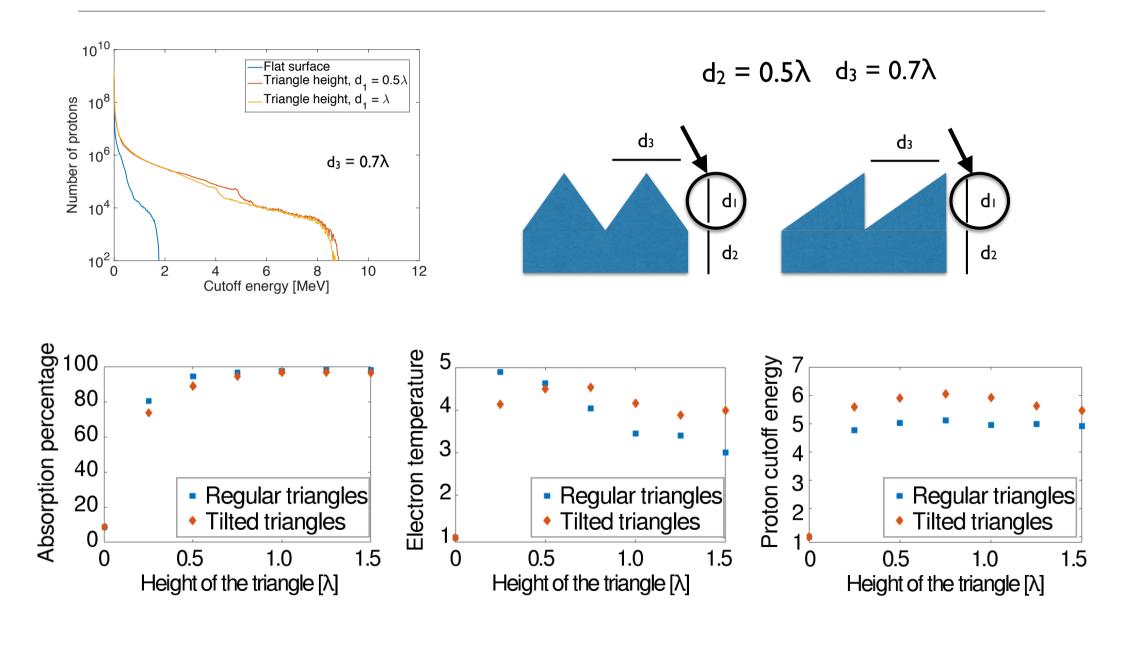


# Dependence on the height of the structure



$$d_2 = 0.5\lambda \quad d_3 = 0.7\lambda$$

# Dependence on the height of the structure

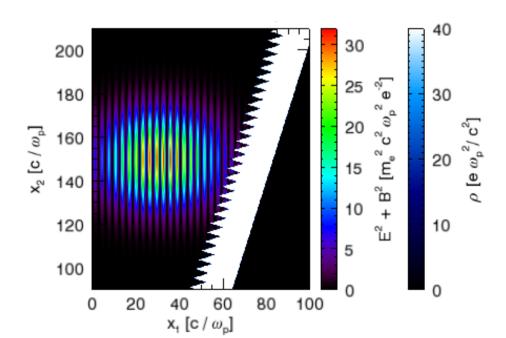


## Angle of incidence

#### Main idea

Ion acceleration is optimized for a set of parameters, depending on the plasma density and laser peak intensity.

We want to obtain an estimate of the outcome in the most optimized situation for oblique incidence.

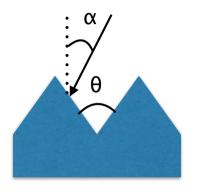


#### **Optimal case**

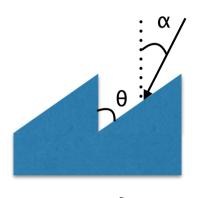
- Incidence: Oblique
- **Structure:** Tilted triangles
- Optimal width: d<sub>3</sub>=0.7λ
- Height with saturation:  $d_1 = \lambda$
- Realistic thickness: d<sub>2</sub>=2λ

# Dependence with the incident angle

$$d_2 = 0.5\lambda$$
  $d_3 = \lambda$ 







 $d_1 = \lambda$ 

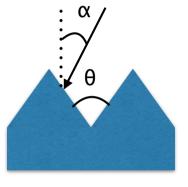
#### What we expect

We expect an asymmetry for the tilted triangles for negative or positive angles.

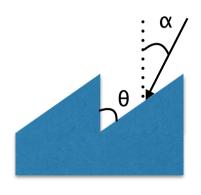
We choose the sizes of the structures to have the same angle  $\theta$ =45°.

### Dependence with the incident angle

$$d_2 = 0.5\lambda$$
  $d_3 = \lambda$ 





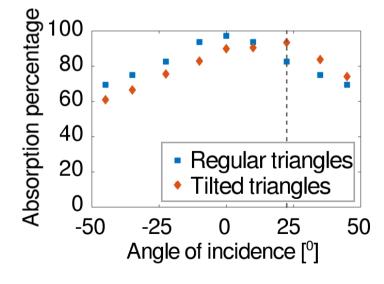


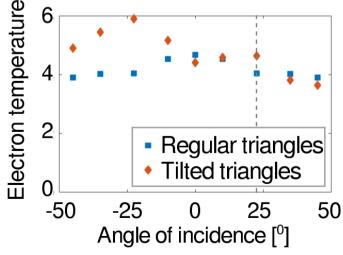
### $d_1 = \lambda$

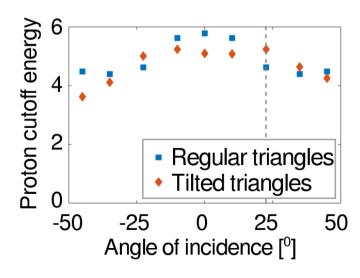
#### What we expect

We expect an asymmetry for the tilted triangles for negative or positive angles.

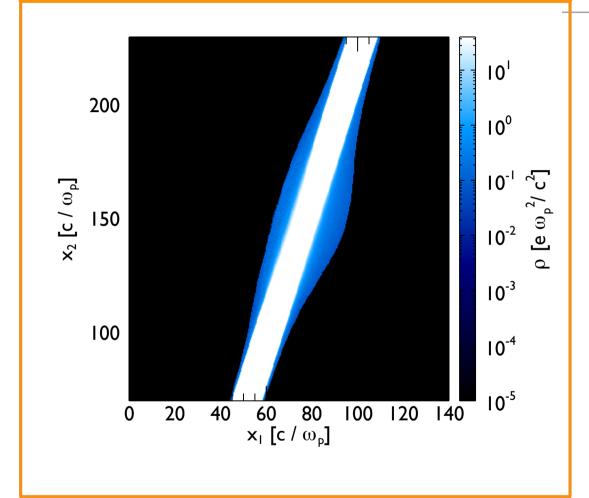
We choose the sizes of the structures to have the same angle  $\theta$ =45°.





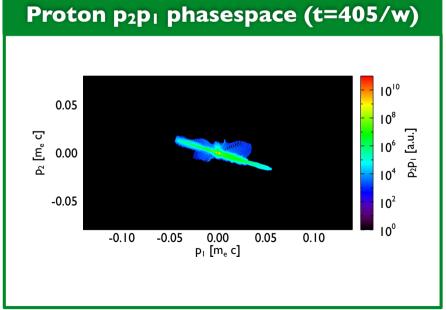


#### Proton charge density (t=405/w)

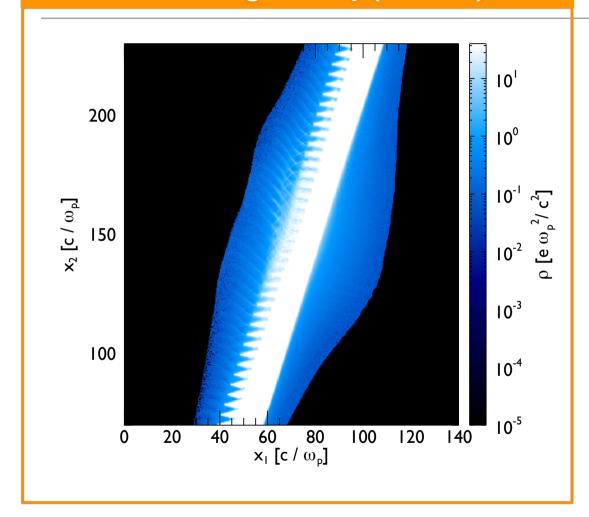


$$\alpha = 17.5^{\circ}$$
  $d_2 = 2\lambda$ 

	Absorption	Proton cutoff	
Flat	6,1 %	1,60 MeV	
Structured	90,6 %	7,72 MeV	
Ratio	14,9	4,8	

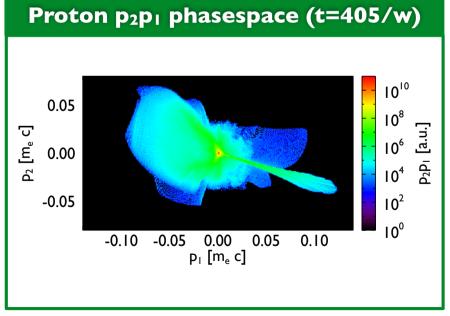


#### Proton charge density (t=405/w)

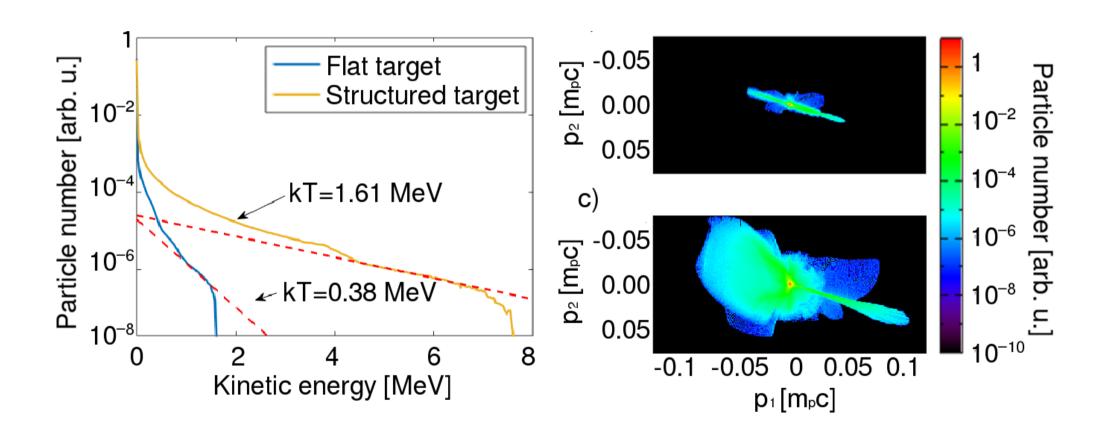


$$\alpha = 17.5^{\circ} \quad d_1 = \lambda \quad d_2 = 2\lambda \quad d_3 = 0.7\lambda$$

	Absorption	Proton cutoff	
Flat	6,1 %	1,60 MeV	
Structured	90,6 %	7,72 MeV	
Ratio	14,9	4,8	



## Optimized proton beam



### Comparison with 3D



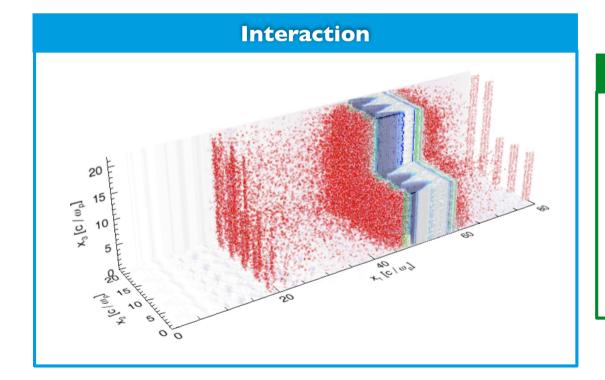
#### Why comparing

We need to know how the results scale from 2D to 3D to see how reliable they are.

We will use slab geometry to compare both cases.

#### Scaling of reflected energy and cutoff

	Regular triangles		Tilted triangles			
	2D	3D	3D/2D	2D	3D	3D/2D
Absorbed	95,4%	91,5 %	0,96	92,3%	89,5 %	0,97
energy	No slab: 97,6 %			No slab: 97,0 %		
Proton cutoff	4.29 MeV	4.28 MeV	0,998	4.50 MeV	4.21 MeV	0,936



#### Simulation setup

Simulation:

Laser:

x axis: 20.4  $\mu$ m in 1600 cells

y/z axis: 2.8 µm in 220 cells

time step: 21.3 as

Plasma

 $a_0 = 4.0$   $n_0 = 6.9 \times 10^{22} \text{ cm}^{-3}$ 

 $\lambda = 0.8 \ \mu m$ length = 18.8 fs  $n_0 = 40 n_c$ particles per cell:  $1 \times 2 \times 2$ 

 $d_1 = \lambda$ 

 $d_2 = 0.5\lambda$ 

 $d_3 = 0.7\lambda$ 

### Comparison with 3D



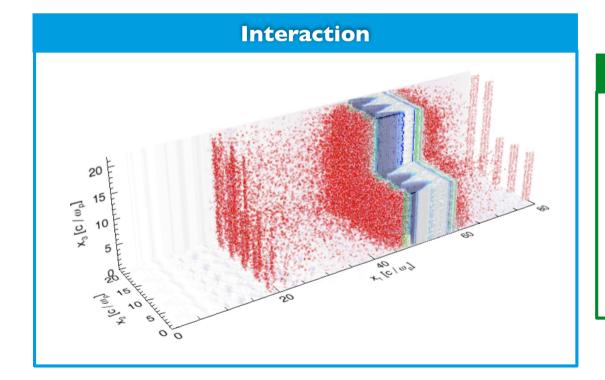
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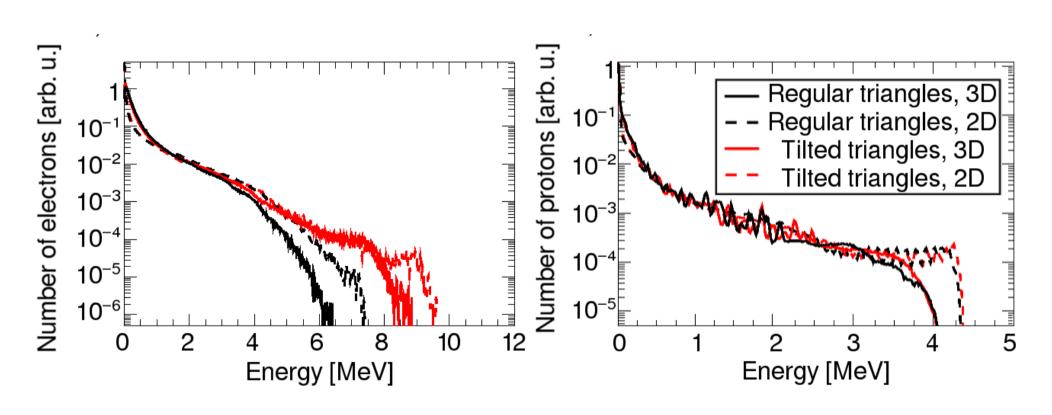
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 $d_1 = \lambda$ 

 $d_2 = 0.5\lambda$ 

 $d_3 = 0.7\lambda$ 

# Comparison 2D vs 3D

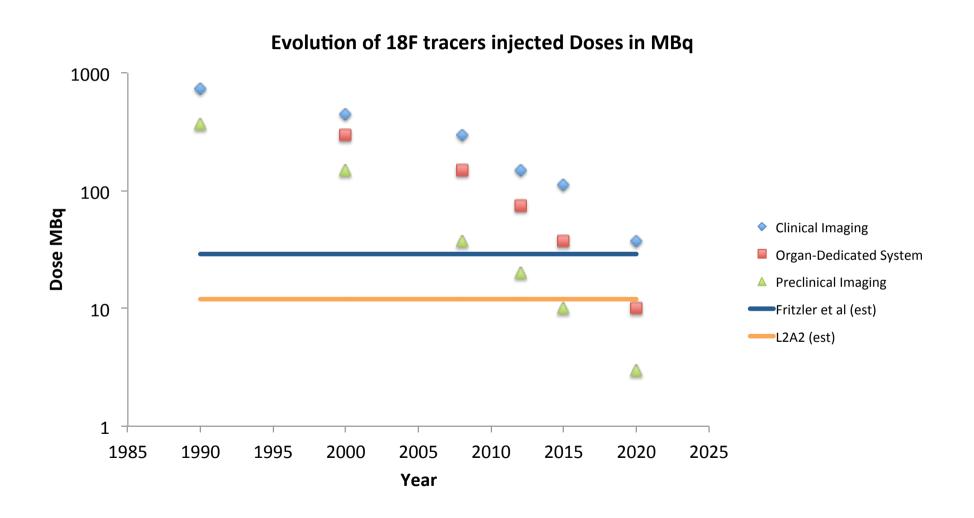


3D:  $3.1 \times 10^{11} p/shot$ 

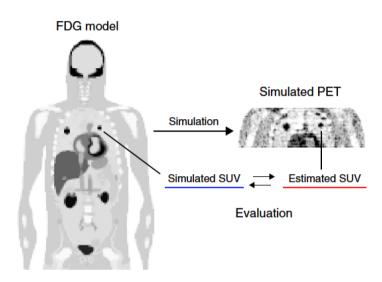
# New diagram for the estimation.

High repetition rate

### The doses are continuously decreasing



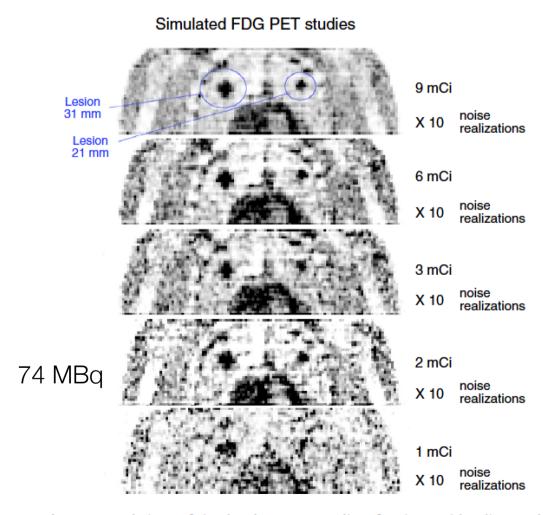
### New imaging techniques



**Fig. 1.** Workflow was based on a realistic framework of multiple simulated FDG-PET studies.

Silva-Rodríguez J, et al. Simulated FDG-PET studies for the assessment of SUV quantification methods. Rev Esp Med Nucl Imagen Mol. 2014. http://dx.doi.org/

10.1016/j.remn.2014.07.006



**Fig. 2.** Coronal views of simulated FDG-PET studies of patients with solitary pulmonary nodules for different injected FDG doses ranging from 9 mCi to 1 mCi.

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# Thanks