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# Hadron acceleration in laser plasma. Perspectives for medical applications



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### Thesis

There ARE numerous reports on intense or/and multi-MeV beams (up to 100 MeV/amu) generated in laser plasma.

There ARE several \_perspective\_ methods and various approaches how to get hardon beams with preset parameters from laser-plasma source.

Laser-based hadron beams ARE widely used in scientific research (f.e for radiography diagnostics of ultra-fast phenomena in plasma, for induced radioactivity and materal science)

Today there IS NO "favorite" approach to provide laser-based hadron source to be \_certainly\_ suitable for conventional technological applications and medical treatment

## Outline



### Radiation therapy with hadrons

Most of the energy deposited in cells by ionizing radiation is channeled into the production of abundant free secondary electrons with ballistic eneries 1~20eV.



// H. Lodish, Molecular Cell Biology (2003)

Cytoplasm can tolerate 250 Gy (Gy = 1 J/g) Hit to Nucleus: 1 to 2 particles kill cell. Issue with radioresistive cells/tumors



#### Hadrons vs X-rays

- The linear energy transfer (LET) from x-ray photons occurs in the course of one single reaction per photon, which results in an exponential attenuation.
- The heavy protons loose their energy due to multiple interactions with the electrons, resulting in Bragg peak in LTE(I).





CT scan of a tumor in the head overlaid by a treatment plan giving the dose in a linear color scale: a scanned carbon beam from two entrance ports (left) is compared to x-ray treatment plan using 9 entrance channels (right).

### A cancer therapy center - construction cost

Proton facility	Synchrotron source, mln\$	Laser-based source (estim), mln\$
Building and shielding	40	2
Accelerator	25	5
Beam delivery to patient	30	10
Carbon facility "factor"	x3	x1.5







#### **Requirements for ion beam therapy**

	Parameter	Unit	Value
1	Maximum energy Protons Carbon ions	MeV MeV/u	250 430
2	Number of particles/sec	pp/s	5×10 <sup>10</sup> 10 <sup>9</sup>
3	Energy spread	-	10-2
4	Discrete step of the beam energy control	MeV	5
5	Bunch duration	ms	400~1000
6	Repetition rate	Hz	PDDS - 0.15 ADDS - 20
7	Dynamic range of control of particle per bunch	=	PDDS - 10 <sup>3</sup> ADDS - 10

// G. Kraft , Prog. Part. Nucl. Phys. 45, S473 (2000)

Treatment possibilies with lower energy hadron sources

Novadays «average record» value for laser accelerated proton energy is in the range of 50-80 MeV

Stopping range of 80 MeV protons in water exceeds 50 mm.

Small tumor <50mm depth from surface of skin:

Ocular disease

(melanoma, age related macular degeneration)

- Paranasal/nasal tumor
- Thyroid cancer
- Laryngeal cancer
- Skin cancer
- Chest cancer
- Superficial LN tumor
- Lung cancer near the chest wall



*Dose:* 40 - 80 Gray distributed over 10-20 fractions -> 1e9-1e10 ions per fraction and few minutes

Spatial and energy control: mm-scale @ 20cm depth -> 200 MeV @ percent level control -> mm pointing (contour shaping) -> 5% position dependent dose control

Clean beam (no other species, X-rays...)

High pulse repetition rate for scanning

### Proton and ion acceleration with lasers - overview

Advantages of mass-limited targets (MLT) are obvious

Maximum ion energy achieved is proportional to laser intensity – confirmed

With laser systems providing > 1e20 W/cm<sup>2</sup> intensities the fastest part of accelerated ions reaches 100 MeVs energies suitable for therapy applications, however <u>the yield</u> of such ions <u>is</u> far below reasonable demand yet.



### Conditions for various ion acceleration mechanisms

Different mechanisms dominate the ion accleration depending on target surface density (or thickness of the foil) and laser parameters. Radiation pressure Laser intensity [W/cm<sup>2</sup>] 10<sup>20</sup> 10<sup>18</sup> 10<sup>16</sup> 1024 Coulomb explosion  $\mathcal{E}_{e}(\tau_{\scriptscriptstyle BBB},\mathcal{P})$ [F9B] a  $\mathcal{P}_{[\Pi B_T]}$ 15 10 5 transparent ao neurelo 0 50 100 150 TNSA  $\tau_{aas}[\phi c]$ Target Normal Sheath Acceleration 10<sup>16</sup> Surface density  $n_e l_0$ 

## Target normal sheath acceleration (TNSA)



// S. A. Gaillard et al., Phys. Plasmas 18, 056710 (2011)

## Target normal sheath acceleration (TNSA)



TNSA acceleration is extremely sensitive to target thickness. The optimisation of target geometry is needed in the range of < 100 nm thickness.



## **TNSA** distinct signatures

I the acceleration dominantly happens in a virtual cathode at the back side of the target with reported energies of up to 67 MeV (protons)

I the dominant species is protons due to their high charge to mass ratio

**I** protons originate from nm-thin surface contamination layer

I the energy spectrum is typically exponentially decaying with a sharp high energy cutoff (at up to 67 MeV for protons)

acceleration of heavier ions requires removal of the contamination layer with target heating

**the target is opaque** to the laser during the whole laser interaction

#### **Radiation Pressure Acceleration (RPA)**



#### Break-out Afterburner (BOA) Mechanism



// L. Yin et al. Physics of Plasmas 14, 056706 (2007)

#### Break-out Afterburner (BOA) Mechanism



Prediction of the maximum carbon  $C^{6+}$  energy and  $t_1$ ,  $t_2$  times vs. Thickness of the target for Trident parameters ( $\tau = 600$  fs,  $E_1 = 80$  J,  $n_0' = 660$ ,  $q_i = 6$  for  $C^{6+}$ ,  $a_0 = 16.8$ )



#### Break-Out Afterburner (BOA) Mechanism



Precise attenuation of target thickness is demanded.

Proton energy of 120 MeV is achieved.

BOA mechanism coupled with CP laser beam provides the conditions for multi MeV proton and sub-GeV Carbon beams with remarkable energy spectra bandwidth.



## Sophisticated target design, and actively-shaped targets

Double-layer targets – High Z to increase electron yield, Low Z – as proton source



## Sophisticated target design, and actively-shaped targets



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# Practical issue with laser pulse contrast

#### Laser pulse temporal profile - key issue in practice



## Toward high quality hadron beams



# In search for convenient, renewable target

# Disadvantages of solid thin foil targets

#### Laser-solid interaction:

Relatively low absorption laser radiation (~10-50%) Target ablation - debris danger for optical elements Not easy to change the target - prevents high repetition rate source Most prospective nm-foil targets are expensive and fragile



Widely used in science but less suitable for applications

# Increase of X-ray yield in cluster targets

Target	O Heβ photon yield, /sr*shot	O Lyα photon yield, /sr*shot		
Bulk SiO2	1.3 E9	0.9 E9		
SiO2 aerogel	4.7 E9	4.3 E9		
CO2 20 bar no clusters	4.1 E9	6.6 E9		
CO2 60 bar μm clusters	3.1 E10	3.0 E10		

// V.P. Efremov et al. Phys. Res. A577 (2007)

Due to Coulomb explosion of each cluster or bead the source radiates almost isotropically in full spatial angle, so provides wide field of view and homogeneous illumination of investigated object.

The targets of submicron or nanometer scale structures provides the increase of X-ray yield up to an order of magnitude



Plasma with density significantly exceed critical laser density and consist of multicharged ions and electrons with keV energies

## The option - submicron gas cluster targets



High efficiency of laser

energy absorption by submicron clusters (90-95%)

Huge total surface of the target = the increase of X-rays and fast ions yield.

Increase of electron density where cluster expansion interacts with each other = X-ray yield increases

- O Almost isotropic ion flow due to Coulomb explosion of clusters
- Q Reduced or even negligible debris production

Easily and fast renewable target = inexpensive realization of Mass Limited Target concept

## The role of laser pulse contrast



# The role of ambient gas

During cluster production in supersonic gas jet a fraction of gas, which turns into clusters is not higher than 30 % (typically it is about 20 % only)!



## Dependence on cluster size



// Y.Fukuda,Y.Akahane,M.Aoyama et al. Laser Part. Beams **22**, 215-220 Cluster size should be >100 nm, preferably >500 nm

Cluster cloud should be of several mm in diameter to realize laser radiation channeling

Special nozzle design and choose of gas pressure and composition are of great importance

Theoretical model of cluster formation has been developed in IMM RAS // A.S.Boldarev et al. Rev. Sci. Instrum., 77, 083112 (2006)

# Frozen nanodroplets

#### Al<sub>2</sub>O<sub>3</sub> substrate

#### H<sub>2</sub>O frozen droplets

#### Mo substrate



Substrate	Absorption coeff.			
	Clear surface	Snow coated		
Molybdenum	0.5	0.5		
Sapphire	0.58	0.94		



Nanoscale solid cluster structure can
 be easily produced by freeze of water condensate at well-polished surface.

• Two times better laser absorption efficiency (94%) is provided

#### // with A. Zigler group, Hebrew University Jerusalem

### Ion acceleration achieved in gas cluster targets





The choose of optimal conditions both for submicron gas clusters creation and for laser beam focalization provides in-order higher energy of generated ion flow.

> 4 TW 30 fs laser pulses absorbed in 1 μm gas clusters initiated fast ion flow with energy ~10 MeV

Fast ion energy linearly dependent on laser intensity

With 10-20 TW laser facility we can expect (10<sup>7</sup> ions/shot) yield of 4-5 MeV ions

# Features of the acceleration methods - summary

#### **Coulomb explosion of cluster targets:**

+ Most easily renewable target, no debris in the interaction area allowing frequent and long lasting ion burst generation

- + Inexpensive realisation of MLT concept
- + Effective transfer of laser energy to ionizing radiation yield
- Broad angular distribution, very broad energy spectra.

#### **Target Normal Sheath Acceleration:**

- + High yield (1e10-1e12 p/bunch),
- + Low transverse emittance (15-20 deg. divergence)
- Broad energy spread, few % efficiency
- Expensive targets especially when sophisticated geometry is applied,
- A lot of debris, doubt with high repetition shots
- Limited use with next generation of ultra-intense lasers

#### **Radiation Pressure Acceleration:**

- + Quais-monoenergetic beams, Low transverse emission
- + High energy hadrons expected
- Demand ultra-high laser contrast and few nm-scale target thickness
- No practical realization yet

### EM-field measurements by proton deflectometry

$$\frac{\delta n_p}{n_p} \simeq -\frac{eL}{2\varepsilon_p M} \int_{-b/2}^{+b/2} \nabla_{\perp} \left( \mathbf{E} + \frac{\mathbf{v}_p}{c} \times \mathbf{B} \right) dx,$$
RCF pack
(a)



# B field of 45 T is measured at ns kJ laser focal spot



# Proton radiography for laboratory astrophysics

Top view

Rear-side

Main laser

Side view

Main laser

**Rear-side** 

plasma

Abla

plasma

Proton radiography method is applied to measure EM field distribution in laboratory astrophysics experiments with colliding plasma flows initiated by kJ ns laser pulses



# Application of cluster based source for ion radiography



Polypropylene, t = 1 μm						
<sup>16</sup> O > 320 keV						
<sup>12</sup> C > 270 keV						

polypropylene foil obtained with the low energy ions:

Images of the 1 micron thickness **Experimental conditions (14-05-08):** Laser: 36 fs, 4.7 TW, 4x10<sup>17</sup> W/cm<sup>2</sup> Target : 90%He + 10% CO<sub>2</sub> (P<sub>gas</sub> = 60 bar) N<sub>shots</sub> = 2800 Samples: CR-39 plates, covered by polypropylene **Distance to the target:** CR-39(2) 140 mm -160 mm CR-39(1) -Angle of irradiation (to the laser beam axis):

-	30°
-	90°
	-

Estimated number of ions: > 10<sup>8</sup> ions/shot



**CR-39** low ions energy observations confirmed isotropic ion distribution from the cluster plasma

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# **Delivery methods**

# Passive dose delivery system (PDDS)

PDDS means the simultaneous irradiation of a whole target (or irradiation of the most part of the target) by a wide ion beam



# Active dose delivery system (ADDS)

ADDS-consecutive irradiation of the target voxels by **the narrow ion beam** using the 3D raster-scan or spot technique: beam is stopped on the voxel up to full accumulation of required dose // G. Kraft, Physica Medica 17, 13 (2001)



# Expositions of biosamples to laser-accelerated hadrons



DNA double-strand breaks induced by the irradiation of laser-accelerated protons,  $\gamma$ -H2AX centers appeared due to *in vitro* irradiation of cancer cells.

// A. Yogo et al. Appl. Phys. Lett. 94, 181502 (2009)

The fraction of surviving cells after the irradiation with the laser-accelerated protons, with the reference to x-ray dose efficiency

// K. Zeil et al. Apl. Phys. B. 110, 437 (2013)

# Conclusion - key issues to be solved

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# Frozen nanodroplets target

*H*<sub>2</sub>*O*-nanodroplets on Sapphire substrate

500 fs

100 fs



• According to X-ray spectroscopy measurements the improvement in fast ion acceleration increases correspondingly to absorption efficiency

#### Лазерный комплекс адронной терапии (ЛКАТ)



# Лазерный комплекс адронной терапии Принцип действия

- Терапия протонными и углеродными пучками признана на сегодня наиболее эффективной и самой прецизионной формой радиационной терапии глубоко расположенных опухолей
- Это связано с особой зависимостью величины энергии, передаваемой тканям, от глубины проникновения адронов в вещество - так называемым "пиком Брегга".
- Положение пика Брегга (глубина расположения в облучаемой ткани) зависит от энергии частиц. Изменяя эту энергию, можно прецизионно сканировать облучаемую область, получая практически однородное распределение дозы облучения с относительно небольшим облучением окружающих здоровых тканей
- Пробег до остановки в теле пациента протонов с энергией 75 МэВ составляет 3 см, а энергией 230 МэВ – 25 см. Лазерные источники быстрых ионов должны удовлетворять жестким требованиям: для целей терапии энергия протонов должна достигать 100 – 250 МэВ, а их количество 10<sup>12</sup> шт.

Доза, поглощенная биологической тканью, в зависимости от глубины проникновения и типа ионизирующего излучения



# Лазерный комплекс адронной терапии Наноразмерные мишени

- Для повышения эффективности нагрева плазмы используют наноразмерные объекты с масштабами на 1-2 порядка меньшими длины облучающих волн
- Мишень получают путем впрыска газовой струи высокого давления через специальное сопло в вакуум. В результате в газовой струе формируются локальные кластерные сгустки твердотельной плотности, состоящие из десятков тысяч молекул, с характерными размерами от 50 до 100 нм и расстоянием между кластерами в единицы мкм
- Поскольку масштаб наноразмерной кластерной структуры на порядок меньше длины волны лазерного излучения, такая мишень является эффективным поглотителем, что увеличивает КПД схемы и повышает энергию ускоряемых частиц
- Наличие огромной внутренней поверхности позволяет на порядки увеличить поток образующихся ионов в сравнении с плоской мишенью
- Простая конструкция и возобновляемость являются существенным преимуществом мишени из газовых кластеров среди различных реализаций концепции наномишеней и мишеней с ограниченной массой (MLT)



Способ образования и характерные параметры кластерной мишени

Эффективное поглощение внутри структуры с масштабом, меньшим длины волны лазера



# Лазерный комплекс адронной терапии Применение

- Механизм терапевтического воздействия разрыв цепочек
- ДНК в ядрах патогенных клеток кулоновским полем быстрых ионов и образующимися в клетке свободными радикалами. После воспроизводства клетки с деформированной ДНК она теряет жизнеспособность.
- Ионный пучок на выходе из ускорителя направляется системой магнитов для осуществления сканирования в плоскости на целевой глубине в пациенте. После завершения сканирования в одной плоскости в пучок вводится поглотитель, уменьшающий энергию пучка для облучения ближе залегающей области опухоли. Процедура сканирования в плоскости повторяется.







CT scan of a tumor in the head overlaid by a treatment plan giving the dose in a linear color scale: a scanned carbon beam from two entrance ports (left) is compared to x-ray treatment plan using 9 entrance channels (right). Even electrons with energies well below ionization thresholds induce substantial yield of single- and double-strand breaks in DNA



# ЛКАТ

# Передовые мировые центры, создающие лазерные ускорители для прикладных задач, срок сдачи в эксплуатацию: 2012-2013 гг.



Проект медицинского центра на основе ЛКАТ: Photo Medical Research Center JAEA, поддержан правительством Японии. http://wwwapr.kansai.jaea.go.jp/pmrc\_en/,

предполагается оказание медицинских услуг.



Создание многофункционального лазерного ускорителя электронов и ионов, в т.ч. для медицинских приложений: Berkley Lab Laser Accelerator (BELLA), Lawrence Berkley National Laboratory,

финансируется Энергетическим агенством США, <u>http://loasis.lbl.gov/</u>

#### Конкурентные технологии:

- линейные ускорители не обеспечивают энергию ионов, достаточную для терапии
- синхротронные ускорители: в соответствии с планом, компания Siemens реализует строительство центров адронной терапии.

Запущен в работу и обслуживает пациентов

#### Heidelberg Ion Therapy Center (Германия),

### SIEMENS

строятся еще 4 центра в Shanghai Proton & Heavy Ion Hospital (Китай),

Particle Therapy Center of Marburg (Германия), Centro Nazionale di Adroterapia Oncologica (Италия), North European Radiooncological Center Kiel (Германия) http://www.medical.siemens.com/webapp/wcs/stores/servlet/CategoryDisplay~q\_catalogId~e\_-11~a\_category

d~e 1033668~a catTree~e 100010,1008643,1033666,1033668~a langld~e -11~a storeld~e 10001.htm



A.Ogura et al., Opt. Lett. 37, 2868 (2012)

# TNSA Static mode ion acceleration in thin layer at the target rear surface



TNSA Dynamic mode

ion acceleration at the front of the plasma cloud expanding to vacuum

$$w \propto \mathcal{E}_{las} au_{las}$$

 $\mathcal{E}_{lpha}=2m_{lpha}c^2w^2$ 

$$\mathcal{E}_{\rm las} = \int \frac{E^2}{4\pi} dV$$

$$N_{lpha} = 2 rac{\mathcal{E}_{las}}{w m_{lpha} c^2}$$

 $\kappa_{\rm eff}=2w$ 

Using these relationships we find that for generation of 5e10 protons per second with the energy of 250 MeV the required 1 Hz laser should have the energy of 3 J. For 30 fs laser pulse duration this corresponds to the laser power about 100 TW . The acceleration efficiency in this case is about 0.7

#### T. Esirkepov, et al, Phys. Rev. Lett. 92 (2004) 175003





lon	Energy(MeV/u)							Int	ensity (pps)
He	100	180	230		-	-	-	-	1.2 x 10 <sup>10</sup>
С	100	180	230	290	350	400	430	-	1.8 x 10 <sup>9</sup>
Ν	100	180	230	290	350	400	430	-	1.5 x 10 <sup>9</sup>
0	100	180	230	290	350	400	430	-	1.1 x 10 <sup>9</sup>
Ne	100	180	230	290	350	400	600	-	7.8 x 10 <sup>8</sup>
Si	100	180	230	290	350	400	600	800	4.0 x 10 <sup>8</sup>
Ar	-	-	-	290	-	400	650	-	2.4 x 10 <sup>8</sup>
Fe		<del>12</del> 18		0.	-	400	500		2.5 x 10 <sup>8</sup>

Heidelberg Ion Therapy Center <u>http://www.klinikum.uni-heidelberg.de/</u>



# Лазерный комплекс адронной терапии Сравнение технологии

Характеристики	Синхротронный ускоритель	ЛКАТ
Количество пациентов, чел./год	1 000 – 1 300	250 – 300
Капитальные затраты на создание ускорителя (без учета оснащения терапевтического центра), млн. руб.	3 500 – 4 000	380
Удельные капитальные затраты на создание ускорителя (без учета оснащения терапевтического центра), тыс. руб. на 1 пациента <sup>[1]</sup>	~110	~70
Потребляемая электрическая мощность, кВт	900 – 1 200	50
Потребляемая электрическая мощность в расчете на 1 пациента, кВт ч <sup>[2]</sup>	~2 000	200
Количество персонала, обслуживающего непосредственно установку, чел.	35 – 40	3 – 4
Трудозатраты обслуживающего персонала в расчете на 1 пациента, чеп./час. <sup>[3]</sup>	7	





#### Shaped foil targets







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Ar	-	-	-	290	-	400	650	-	2.4 x 10 <sup>8</sup>
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