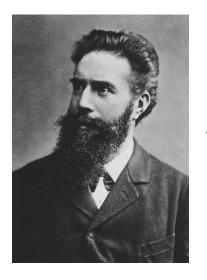
Improving the Outcome of Lung Cancer with Advanced Technology: Photon, Proton and Carbon

> Hak Choy, MD UT Southwestern Dallas, Texas

### 1895 – A New Kind of Ray



Wilhelm Röntgen

EINE NEUE ART

#### STRAHLEN.

¥on

DE W. BÖNTGEN, 8. 0. PROFESSOR AN DER R. UNIVERSITÄT WÜRZBURG

WÜRZBURG. VERLAG UND DRUCK DER STAHELSCHEN K. MOF- UND UNIVERSITÄTS-BUCH- UND KUNNTHANDLUNG. Rode 1895.

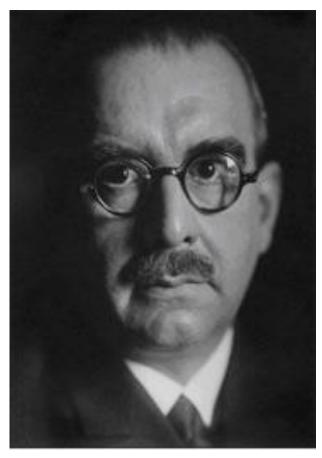
### 1908 - Stockholm Method of Hypofractionation Using Brachytherapy



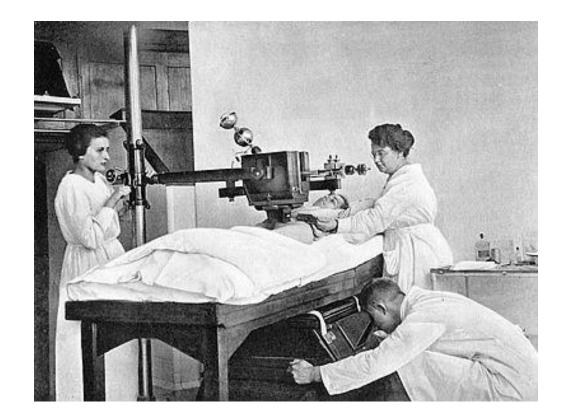
Gösta Forsell



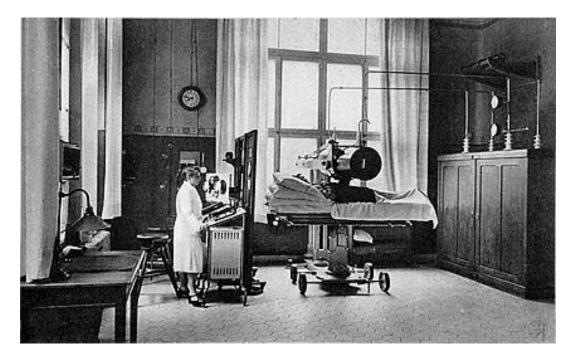
### 1914 – Erlanger Method of Hypofractionation using Teletherapy



Hermann Wintz



### 1920 - Cervix Cancer is "Cured" by Hypofractionated Brachy- and Teletherapy



Gynecological specialist congress - a participant shouted,

"Cancer is defeated ..."

## Late 1920's – The Sky Fell



LATE radiation toxicity: ulceration, denervation, devasculization, stenosis, fibrosis, devitalization

# Why did the sky fall?

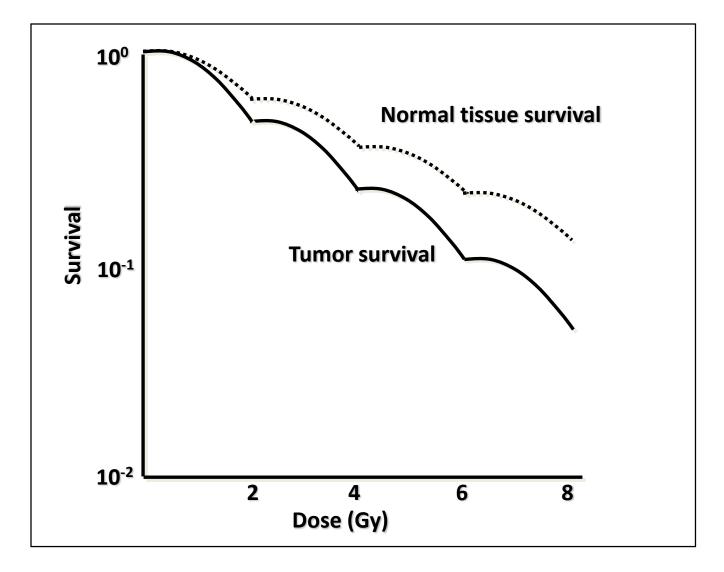
- Technology problems
  - Very low energy beams (most dose into the skin)
  - Crude guidance
  - Poor understanding of radiation interactions (unable to represent dose



# Why did the sky fall?

- Technology problems
  - Very low energy beams (most dose into the skin)
  - Crude guidance
  - Poor understanding of radiation interactions (unable to represent dose
- Biology problems
  - As with tumor, normal tissues poorly tolerant of radiation therapy
- Clinical problems
  - Crude understanding of tumor location
  - Normal tissues extensively irradiated

# **Traditional Radiobiology**



### US Pioneers Champion Protracted Fractionation



**Gilbert Fletcher** 



Juan Del Regato



Henry Kaplan



Franz Buschke



**Isodore Lampe** 

### Fletcher, Kaplan, Lampe, Del Regado, and Buschke's Toolbox

Mostly 1-D and 2-D teletherapy



### Tools that Fletcher Didn't Have



- Stereotactic targeting
- 3-D conformal avoidance
- IMRT
- 4-D motion assessment
- Motion control
- Image guidance

-ALL FACILITATING STEREOTACTIC ABLATIVE (SABR) AND IMAGE-GUIDED HYPOFRACTIONATED RADIOTHERAPY

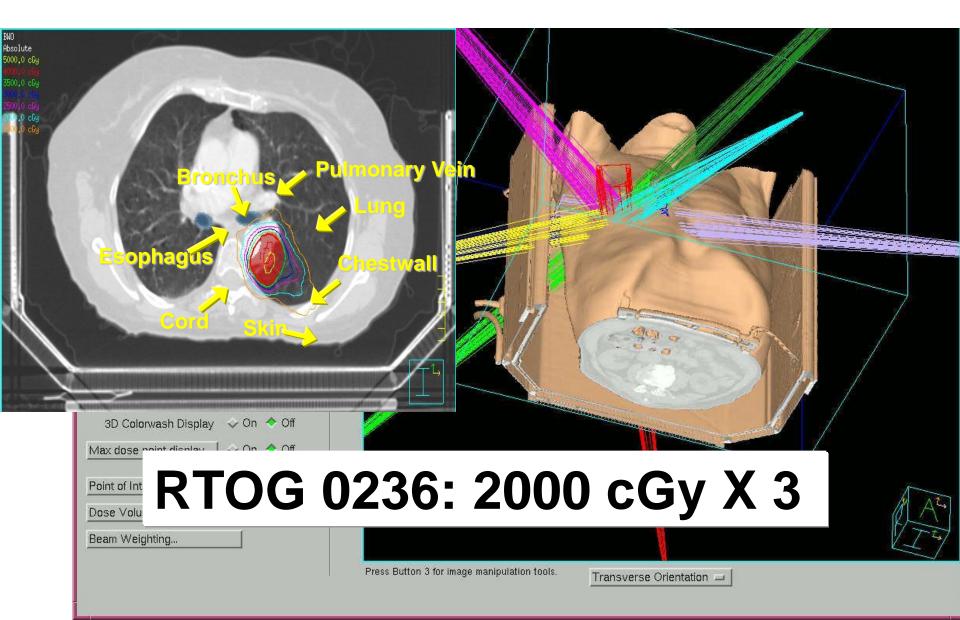
## The Advancement of Radiation Therapy Technology

#### Early Stage NSCLC: SBRT

#### LAStage NSCLC: IGRT

Advanced Stage NSCLC: SBRT

### **Stereotactic Body Radiation Therapy**



#### RTOG 0236: Local Control #/1 ++ Local Control (%) 36 month local control = 98% (CI: 84-100%) 1 failure within PTV, 0 within 1 cm of PTV Fail: Total: $\mathbf{O}$

Months after Start of SBRT

Patients at Risk

Timmerman: ASTRO 2009, 11/2/2009 Chicago

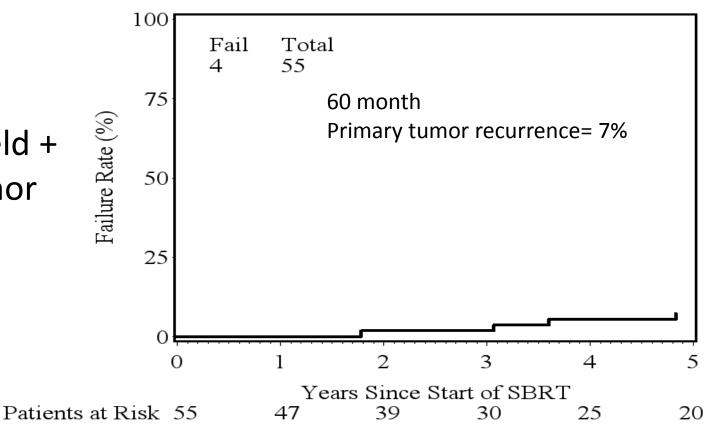


Online article and related content current as of July 15, 2010.

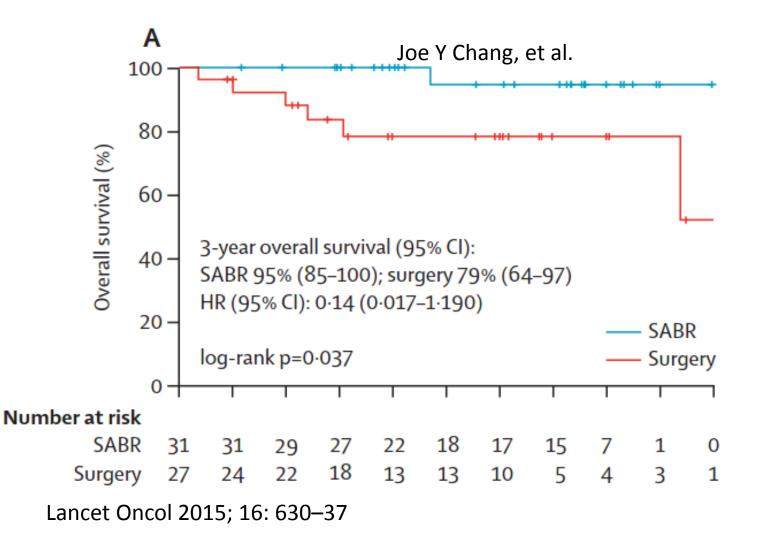
RTOG 0236 Primary (In-field + Marginal) Tumor Recurrence

### Stereotactic Body Radiation Therapy for Inoperable Early Stage Lung Cancer

Robert Timmerman, MD; Rebecca Paulus, BS; James Galvin, PhD; Jeffrey Michalski, MD; William Straube, PhD; Jeffrey Bradley, MD; Achilles Fakiris, MD; Andrea Bezjak, MD; Gregory Videtic, MD;David Johnstone, MD; Jack Fowler, PhD; Elizabeth Gore, MD; Hak Choy, MD



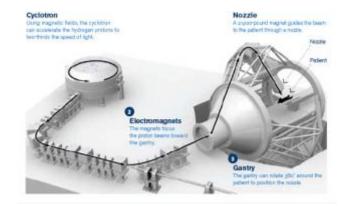
Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomized trials



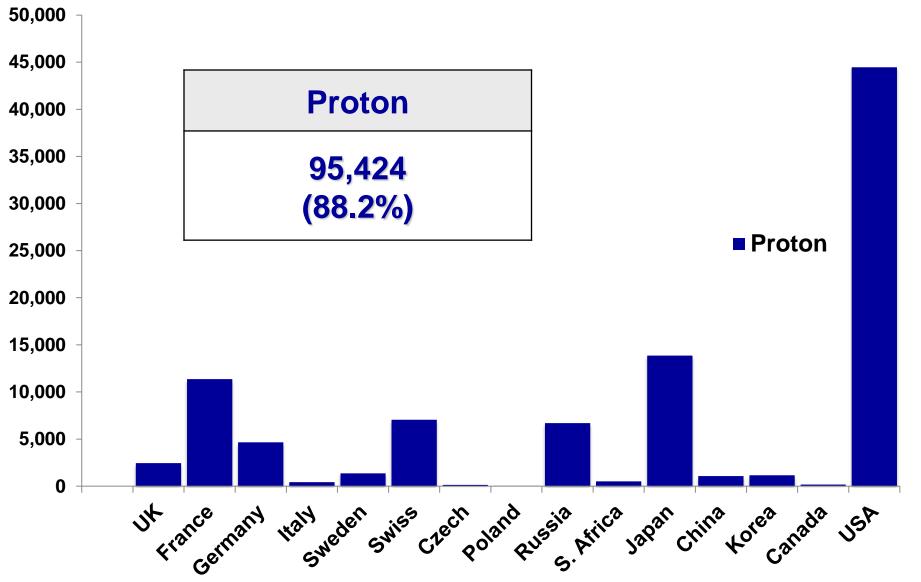
#### Radiation Oncology – Beyond Photon

- Conventional Therapy
  - Standard Care
- Proton therapy
  - The Recent Technology



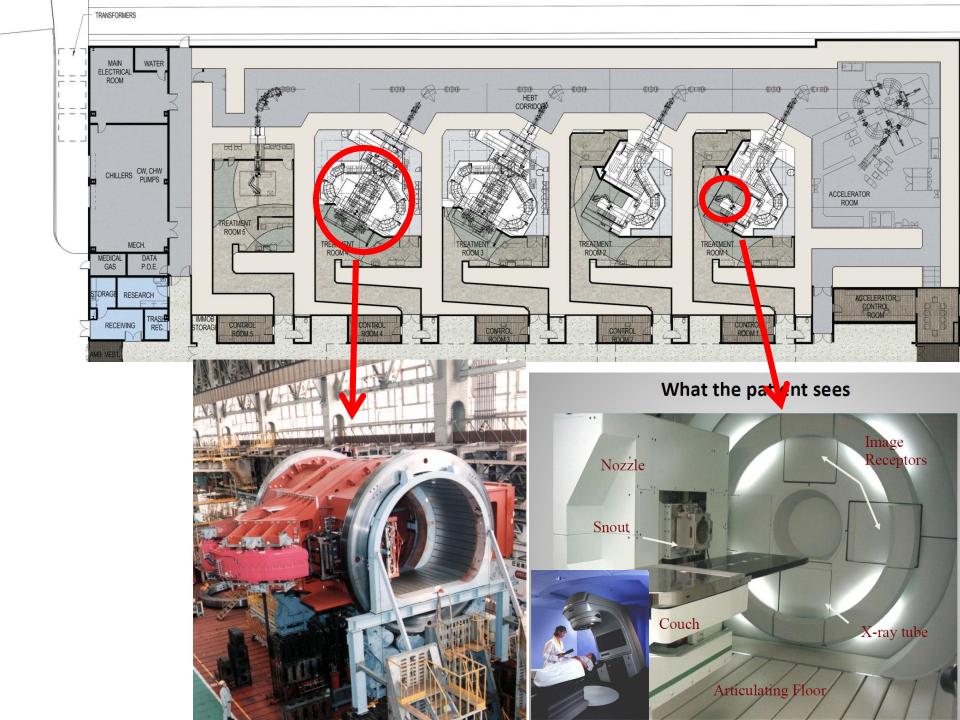


#### Number of patients treated with Protons in the world



Proton Therapy: What is it ? What's the big deal about it ? TAEL 

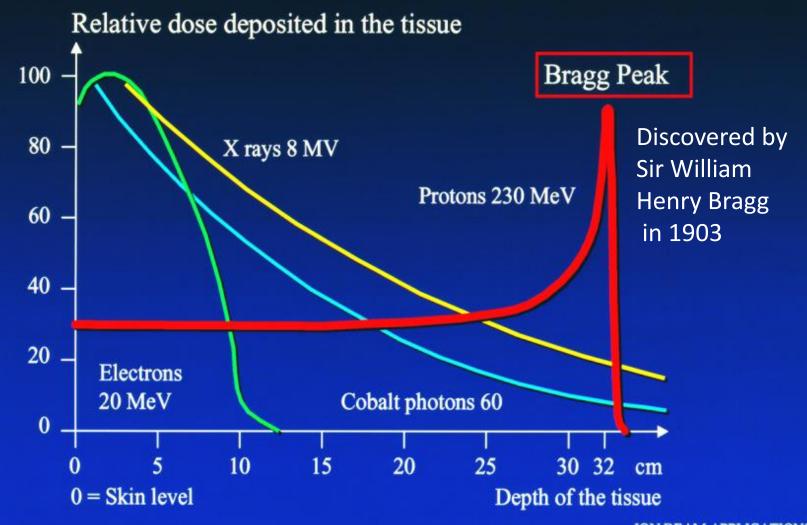
It's a Big machine ! 13 m diameter 190 tons SAD ≥ 2.7 m



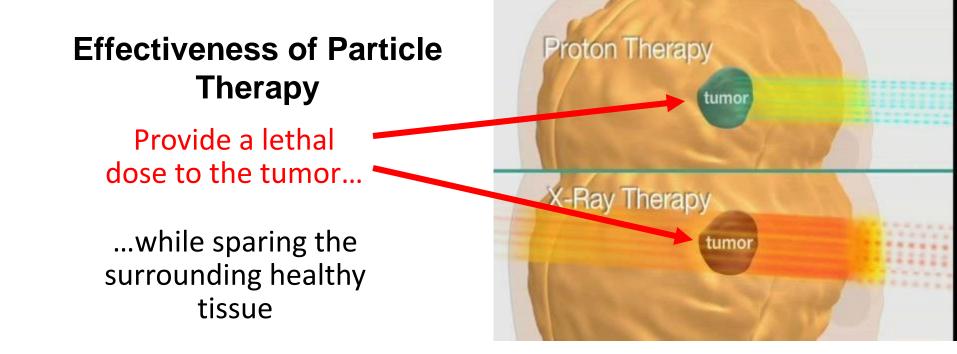
# How Proton is different than X-rays/Photon ?

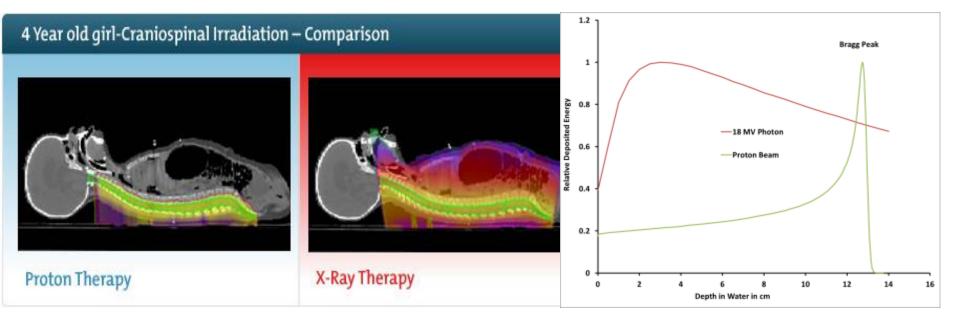
Mostly in the Physical property Not much difference in Biology!

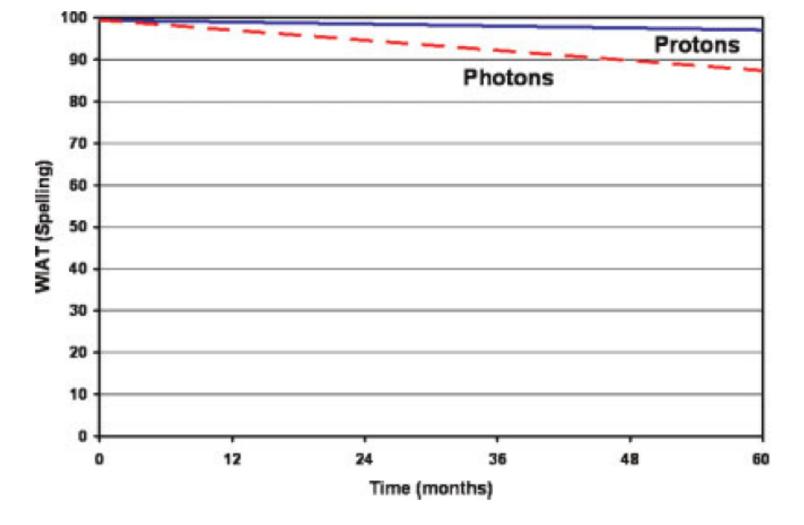
# **Dose Distribution Advantage**



ION BEAM APPLICATIONS

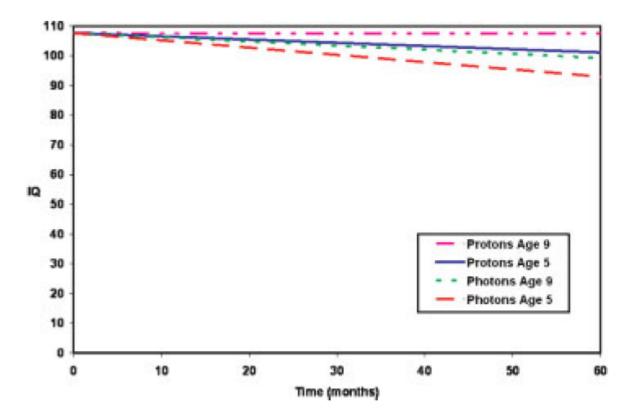






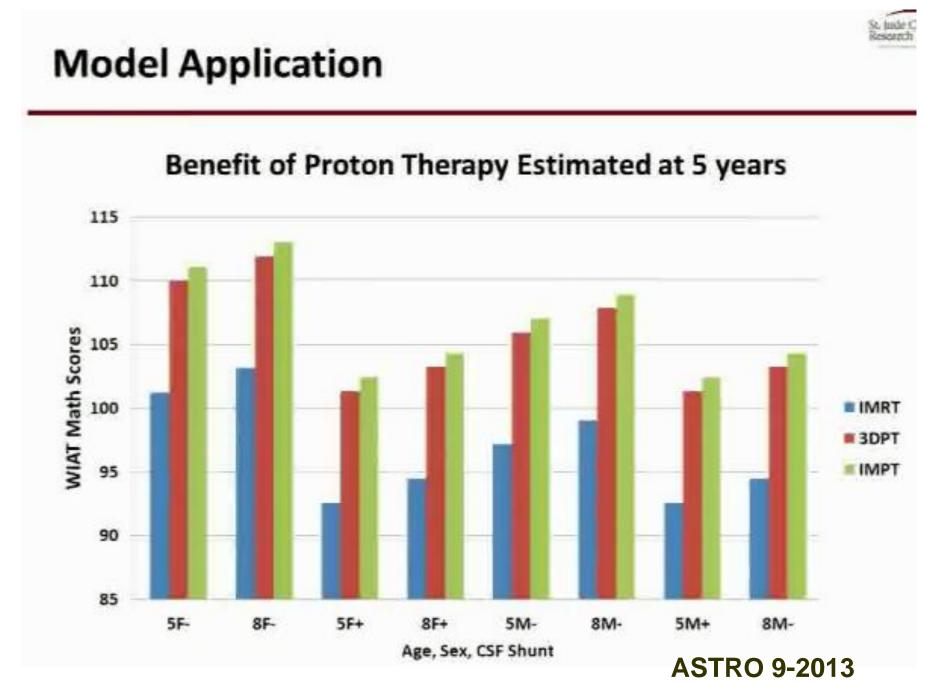
Estimated WIAT spelling score for patients with optic pathway Fig. 3. glioma planned for treatment with scanning proton beam (blue line) and conformal photon radiation therapy (red/dashed line). [Color figure can be viewed in the online issue, which is available at www.interscience. wiley.com.]

#### **Pediatr Blood Cancer 2008;51:110–117**



**Fig. 5.** Estimated IQ for patients ages 5 and 9 with craniopharyngioma planned for treatment with scanning proton beam therapy and conformal photon radiation therapy. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

#### Pediatr Blood Cancer 2008;51:110–117



# General Hypothesis of using Proton Beam for Lung Cancer

1. Proton therapy can significantly reduced the volume of lung/heart exposed to radiation and sparing of normal tissues compared to photon therapy: Potential reduced Toxicities and perhaps better survival.

 Higher dose conformity of dose distributions can be exploited to escalate tumor dose:
 Possible better tumor control.

# Long-term outcomes after proton therapy, with concurrent chemotherapy, for stage II–III inoperable non-small cell lung cancer

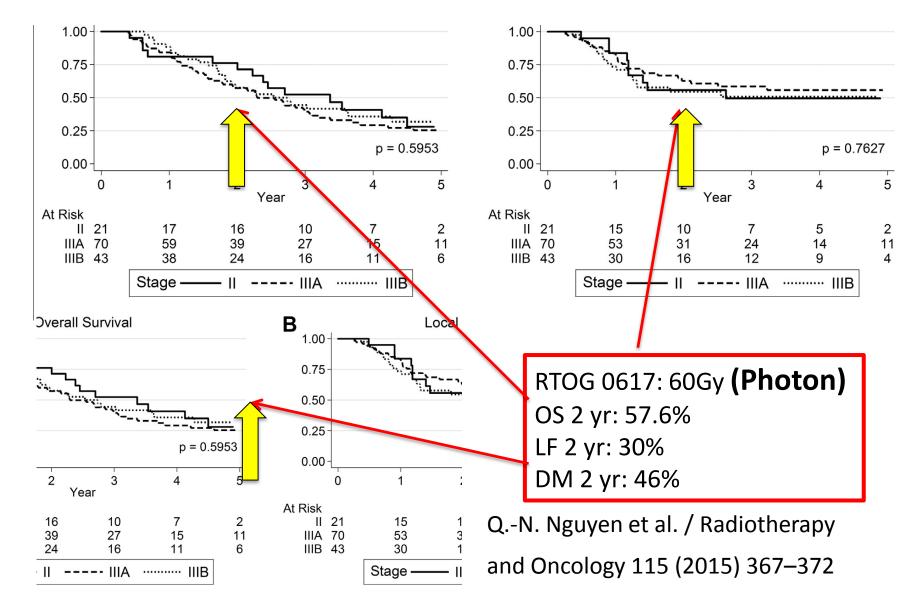
Type of Toxicity	No. of patients experiencing toxicity (%)				
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Dermatitis	74 (55)	33 (25)	19 (14)	8 (6)	0
60-66 Gy(RBE)	14 (61)	5 (22)	2 (9)	2 (9)	0
70-72 Gy(RBE)	19 (56)	9 (26)	4 (12)	2 (6)	0
74 Gy(RBE)	41 (52)	19 (25)	13 (17)	4 (5)	0
Esophagitis	69 (51)	25 (19)	33 (25)	6 (4)	1 (1)†
60-66 Gy(RBE)	10 (43)	3 (13)	8 (35)	2 (9)	0
70-72 Gy(RBE)	24 (71)	6 (18)	3 (9)	1 (3)	0
74 Gy(RBE)	35 (45)	16 (21)	22 (29)	3 (4)	1 (1)
Radiation pneumonitis	68 (51)	35 (26)	29 (22)	2 (1.5)	0
60-66 Gy(RBE)	14 (61)	5 (22)	4 (17)	0	0
70-72 Gy(RBE)	20 (6)	9 (26)	5 (15)	0	0
74 Gy(RBE)	34 (44)	21 (27)	20 (26)	2 (3)	0

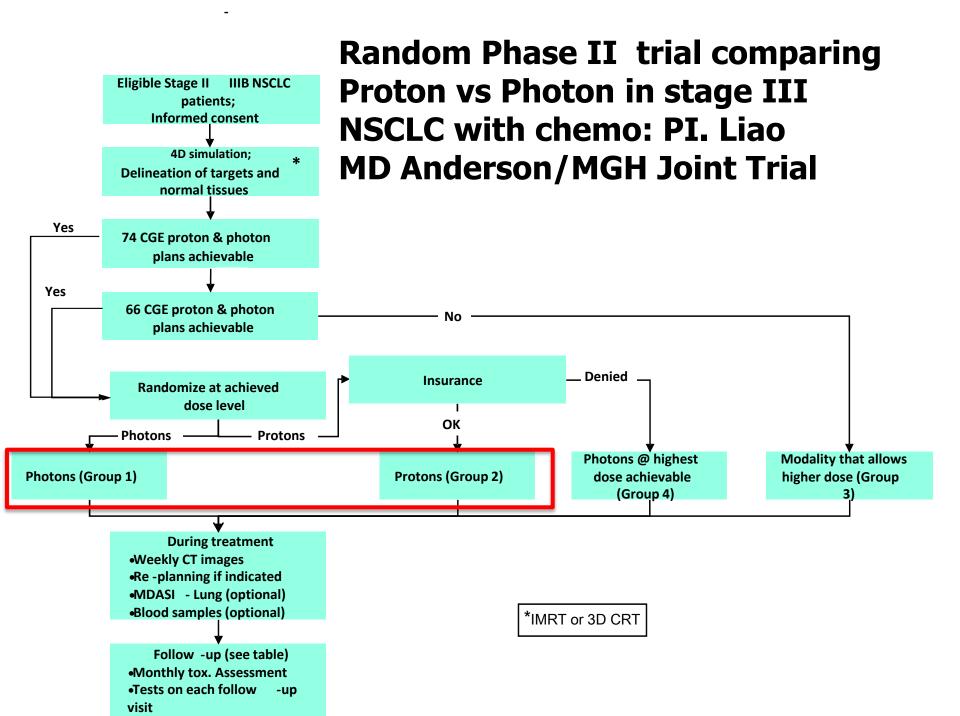
Q.-N. Nguyen et al. / Radiotherapy and Oncology 115 (2015) 367–372

True aided Pickas's succe test

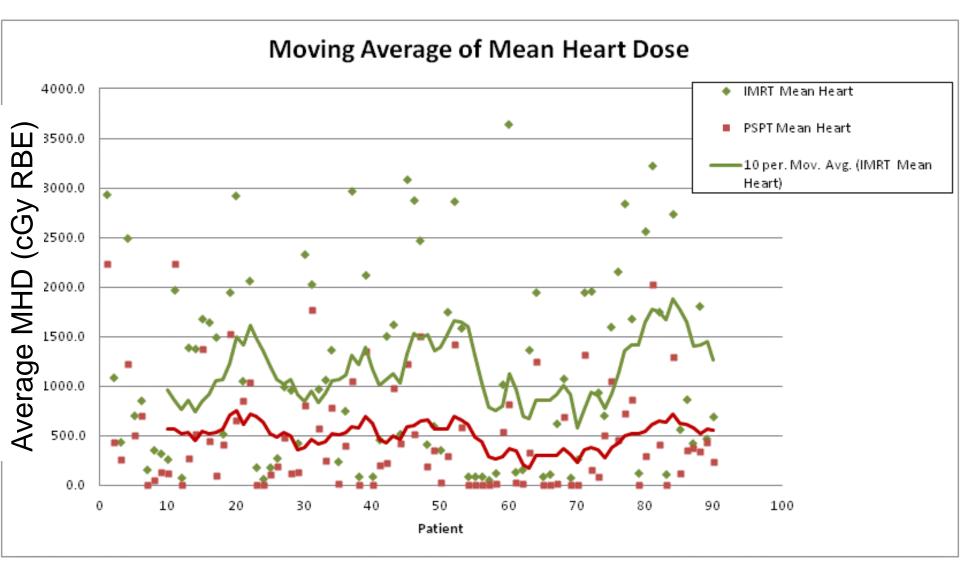
 Proton therapy can significantly reduced the volume of lung/heart exposed to radiation and sparing of normal tissues compared to photon therapy: Potential reduced Toxicities → improve survival ?"

#### Long-term outcomes after proton therapy, with concurrent chemotherapy, for stage II–III inoperable non-small cell lung cancer





#### **IMRT vs. PSPT - Latest Results**



Personal Communication From Dr Liao 2015

How can we demonstrate the Proton Radiotherapy is Superior to Intensity Modulated Radiotherapy (IMRT) ?

- Understanding the impact on biologicallyeffective proton dose distributions delivered to the patient
- linear energy transfer (LET) guided plan optimization with intensity modulated proton therapy (IMPT)
- 3. Minimize the uncertainties: Range uncertainty, intra-fractional motion, inter-fractional anatomic changes
- 4. Randomized Phase III trials in certain Tumor

#### **RTOG 1308**

#### Phase III Randomized Trial Comparing Overall Survival after Photon versus Proton Radiochemotherapy for Inoperable Stage II-IIIB NSCLC

SCHEMA

Stage Arm 1: Photon 1. dose—Higher 2. IIIA achievable dose 3. IIIB between 60-70 Gy, R once daily plus S GTV Volume A platinum-based **T** 1. ≤ 130 cc N doublet **R** 2. > 130 cc chemotherapy\* D Α Ο Т Histology M Arm 2: Proton 1. Squamous dose—Higher F Non-2. Z achievable dose Y Squamous E between 60-70 Gy (RBE), once daily Neoadjuvant plus platinum-Chemo based doublet 1. No chemotherapy\* 2. Yes

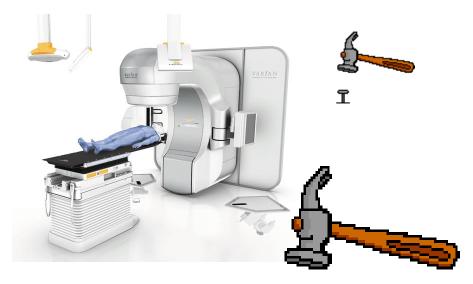
Both Arms:

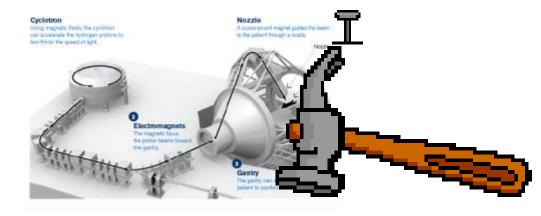
Consolidation chemotherapy x 2 is allowed\*

Target Accrual: 560, Accrual as of 1/15: 48

#### Radiation Oncology – Beyound Photon and Proton

- Conventional Therapy
  - Standard Care
- Proton therapy
  - The Recent Technology

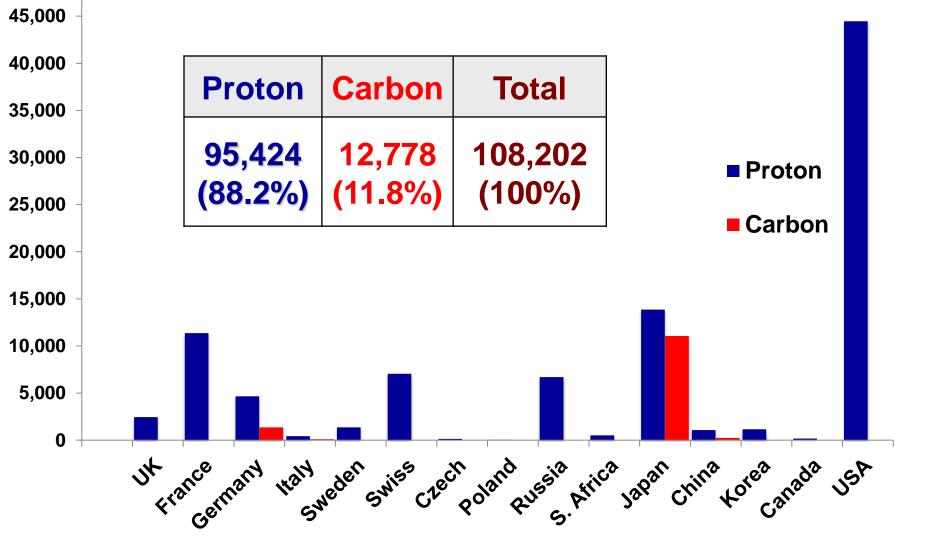




- Heavy Ion Therapy
  - The Most Advanced Technology

### Number of patients treated with Protons and C-ions in the world

50,000



## World Wide Heavy Ion Therapy Centers

#### Operational (11) 🛆

Austria MedAustron, Wiener Neustadt China Fudan Univ CC, Shanghai China IMP-CAS, Lanzhou Germany HIT, Heidelberg Germany MIT, Marburg Italy CNAO, Pavia Japan HIMAC, Chiba Japan HIBMC,Hyogo Japan GHMC, Gunma Japan SAGA-HIMAT, Tosu Japan i-ROCK, Kanagawa

#### Under Construction(5)

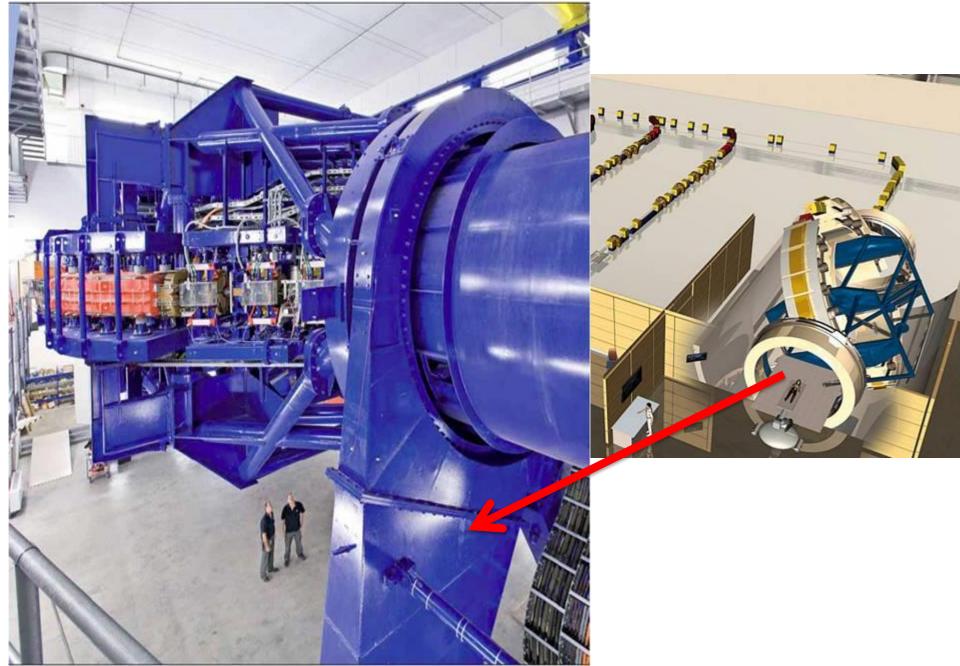
China HITFiL, Lanzhou China Another Center, Lanzhou Japan, Osaka Japan, Yamagata South Korea KHIMA, Busan

#### Advanced Planning(4)

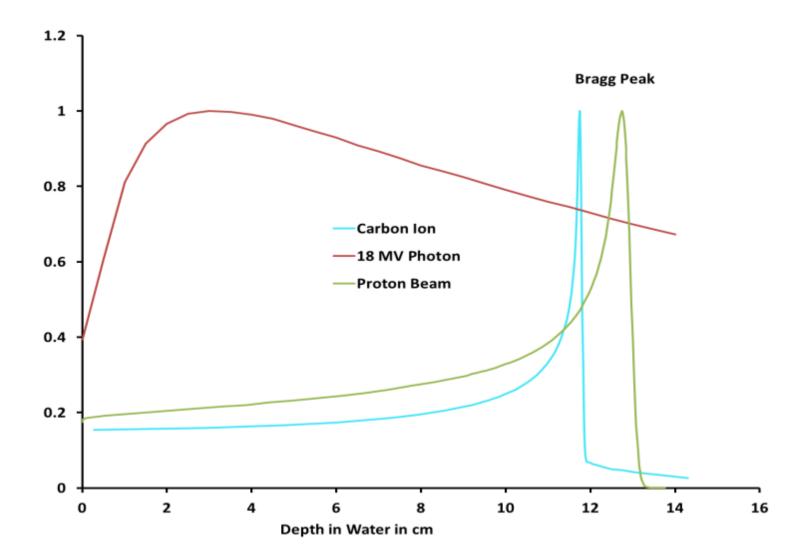
Japan Okinawa Taiwan, CMU Taiwan, Taichung Univ South Korea, Yonsei University

Total : 20

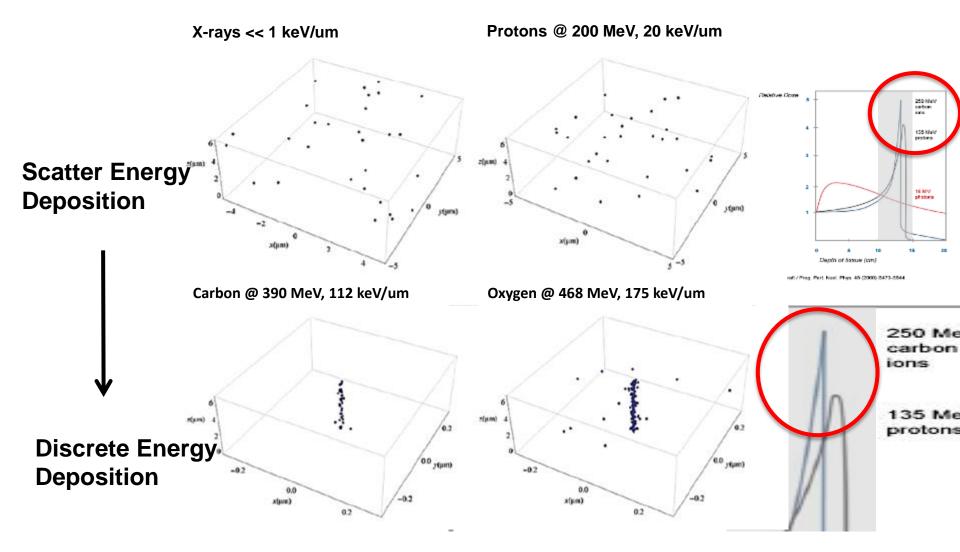
### It's the Biggest Radiation Therapy Machine



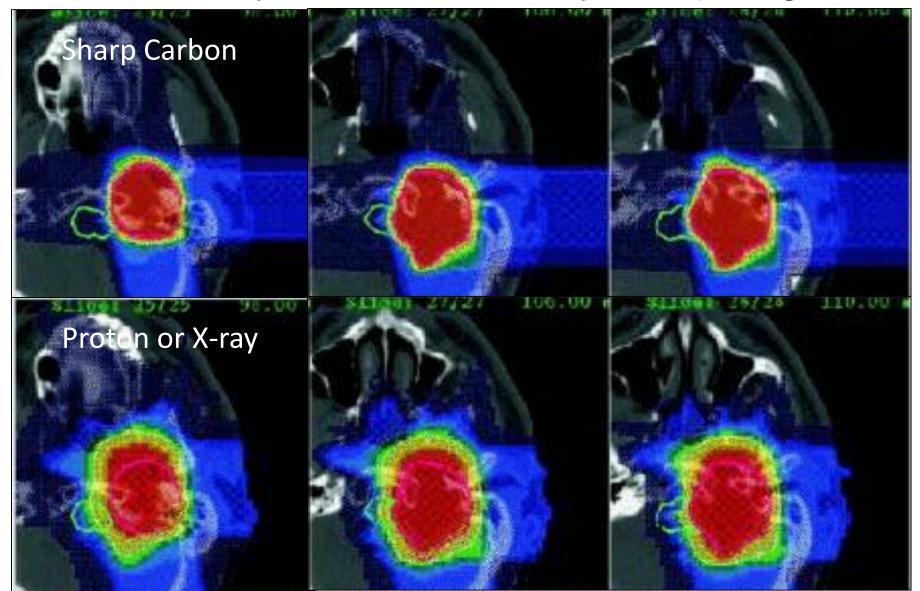
# Perhaps, we can do better with Heavy Ion Therapy (Carbon) !



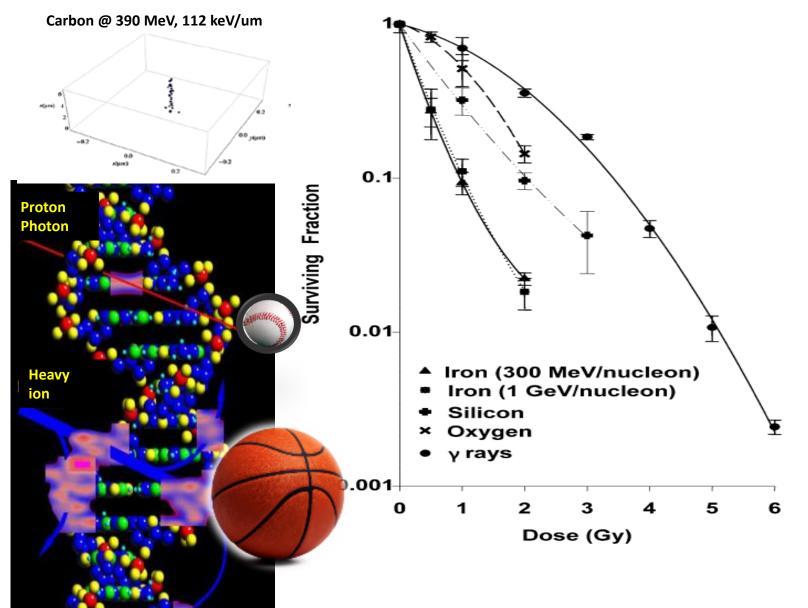
• Energy deposition patterns become more discrete



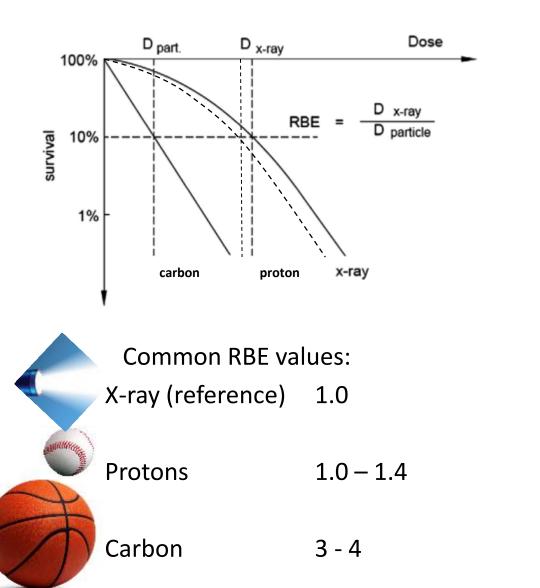
### 3) Heavy lons – have very sharp edges

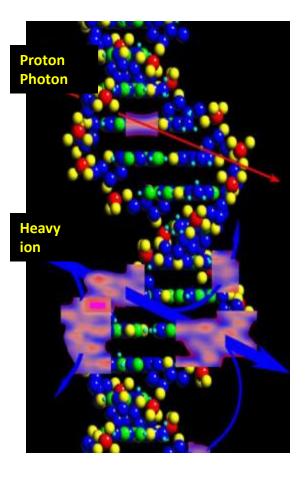


# Discrete patterns of energy deposition result in clustered DNA damage and greater cell killing

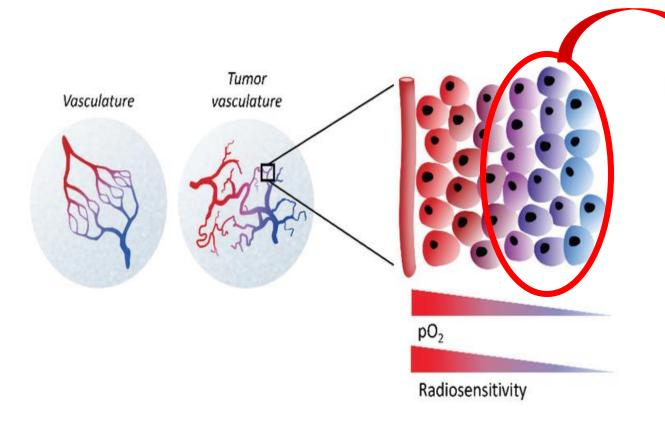


Enhanced cell killing described by Relative Biological Effectiveness





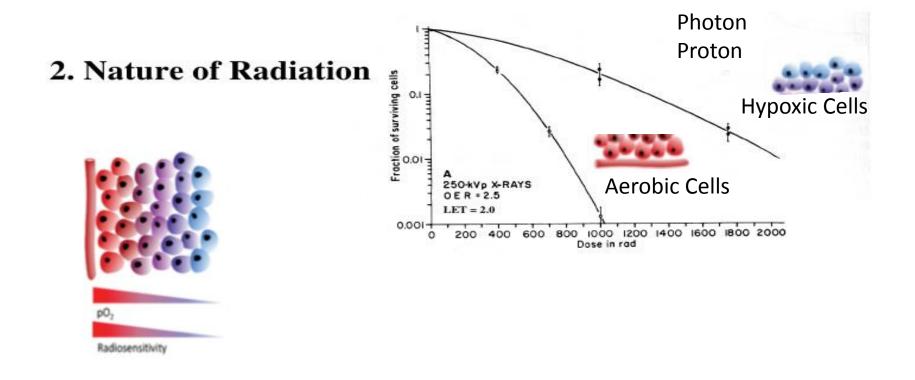
# Heavy charged particles can overcome radioresistance due to hypoxia



Hypoxic tumors show:

- Increased aggressiveness
- Resistance to therapy
- Increased metastasis
- Poor patient prognosis

# Heavy charged particles can overcome radioresistance due to hypoxia



## World Wide Heavy Ion Therapy Centers



**USA** Berkeley Nat. Lab, last patient treated1993

#### Operational (11) 🛆

Austria MedAustron, Wiener Neustadt China Fudan Univ CC, Shanghai China IMP-CAS, Lanzhou Germany HIT, Heidelberg Germany MIT, Marburg Italy CNAO, Pavia Japan HIMAC, Chiba Japan HIBMC,Hyogo Japan GHMC, Gunma Japan SAGA-HIMAT, Tosu Japan i-ROCK, Kanagawa

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#### Advanced Planning(4)

Japan Okinawa Taiwan, CMU Taiwan, Taichung Univ South Korea, Yonsei University

Total : 20

# Ion Beam Initial clinical Trials at LBNL-UCSF, 1975–1992





Prof. Joseph Castro, UC San Francisco conducted the LBNL clinical trials in1975. Almost 3000 patients were treated until 1992.



Prof. T. Phillips

Prof. J. Quibby

Prof. G. Chen Dr. E. Blakely

## Heavy Ion Therapy at LBNL(1975~1992)

- Heavier ions were the most effective in : salivary, bone & soft tissue, and bile duct tumors. slow growing tumors, hypoxic tumors.
- Optimal ion species for clinical use :
  - somewhere between lithium and oxygen, and <u>carbon ions might be the best.</u>

																	2 He 4.0026
4 Be 9.0122												5 B 10.811	6 C	nitrogiin 7 <b>N</b> 14.007	8 0 15,999	fluorine 9 F 18.998	10 10 Ne 20.180
12 Mg 24.305			-				100					13 AI 26.962	14 Si 28.086	15 P 30.974	16 S 32.065	17 CI 35.453	18 Ar 39.948
20 Ca 40.078		21 Sc 44.966	22 <b>Ti</b> 47.867	23 V 50.942	24 Cr 51.996	25 Mn 54.938	26 Fe	27 Co	28 Ni 58.093	29 Cu 63.540	30 Zn	31 Ga	32 Ge 72.61	33 As 74.922	34 Se 78.96	35 Br 79.904	83.80
38 Sr 87.62 barium		39 Y 88.900 Iutetium	40 Zr 91.224 hotnourn	41 Nb 92.906 tantakm	42 Mo 95.54 tungsten	43 Tc	44 Ru 101.07 osmium	45 Rh 102.91 Holum	46 Pd 106.42 platinum	47 Ag 107.87 9083	48 Cd 112.41 Everoury	49 In 114.82 mailium	50 Sn 118.71 kiad	51 Sb 121.76 bismuth	52 Te 127.60 polonium	53   126.90 astatine	54 Xe 131.29 radon 86
	4 Be 20122 12 Mg 24 305 coldum 20 Ca 40.078 strondum 38 Sr 87.62	4 Be 20122 12 Mg 24 305 Calesum 20 Ca 40.078 stroetdum 38 Sr 87.62 barlum	4 Be 20122 12 Mg 24.305 coldum 20 Ca 40.078 8condum 21 Scc 44.966 9tftium 38 Sr 87,62 68.906 barlur 40.066 9tftium 39 Sr 87,62 68.906 barlur 10 10 10 10 10 10 10 10 10 10	4 Be 20122 12 Mg 24 305 coldum 20 Ca 40.078 strontum 38 Sr 87.52 57.55.55 57.5	4         Be           20122         2305           Mgg         scandkim         Mariaim         variadium           20         21         22         23           Ca         21         22         23           Sc         Ti         V         38           38         39         40         41           Sr         Y         Zr         Nb           87.62         50.942         incohum         incohum           39         40         41         Nb           Sr         Y         Zr         Nb           87.62         01.224         92.906         intatum	4         Be           20122         20122           Mgg         scandum         ttanium         vanadum           20         21         22         23         24           20         21         22         23         24         24           Ca         44.966         47.867         50.942         51.996           Strontum         39         40         41         42           Sr         9         Y         Zr         Nb         Mo           87.62         68.906         91.224         92.906         95.54           barlum         Methum         huteflum         turtakum         turgstein	4         Be           20122         305           Oxidation         scandium         titanium         variadium         chromsum         nanganiese           20         Ca         21         22         23         24         25           Ca         44.966         47.867         50.942         51.996         54.939           38         Sr         39         40         41         42         43           Sr         Y         Zr         Nb         Mo         Tc         100           87.62         89.996         91.224         92.996         95.94         198         198	4         Bee 20122           12         Mgg 24.305           Mgg 24.305         scandkum         Mamium         vanadkum         chronsum         manganese         iron           20         21         22         23         24         25         26           Ca         44.966         47.867         50.942         51.996         54.938         56.845           Strontkam         39         40         41         42         43         44           Sr         Y         Zr         Nb         Mo         Tc<	4         Be 30122           12         Mg 305           Mg 24 305         iscansture           12         Mg 305           20         21         22         23         24         25         26         27           Ca 40.078         Sc         Ti         V         Cr         Mn         Fee         Co           38         Sr         39         40         41         42         43         44         45           87.62         Y         Zr         Nb         Mo         Tc         Ru         Rh           87.62         Metlam         11.224         32.906         95.54         1940         101.07         102.91           57.62         barlum         Metlam         functium         tuntatum         tuntatum         tuntatum         ontextum         ontextum         ontextum         00000         101.07         102.91	4         Be 20122           12         Mg 24 305           Mg 24 305         12           Ng 20         12           20         21         22         23           20         23         24         25         26         27         28           Sc         Ti         V         Cr         Mn         Fee         Coo         Ni           40.078         Storntam         100.41         100.41         100.41         100.41         100.41           38         Sr         39         40         41         42         43         44         45         46           Y         Zr         Nb         Mo         Tc         Ru         Rh         Pd           38         Sr         Y         Zr         Nb         Mo         Tc         Ru         Rh         Pd           87.62         68.900         91.224         92.906         95.541         1981         101.07         102.91         106.42           54.41m         Interburn         Interburn         Interburn         100.42         100.42         100.42         100.42         100.42         100.42         100.42         100.42	4 Be 20122         4 20122           12 Mgg 24.305 coldum 20 Ca 40.078 Strontum 38 Sr         scandkum 21         thankum 22         vanadkum 23         chronsum 24         manganese 25         iron 26         coluit 27         rickel 28         copper 29           Ca 40.078 Strontum 38         Sc         Ti 24         V         Cr         Mn         Fee 56.845         28.003         58.603         63.546           44.966         47.867         50.942         51.996         54.938         56.845         58.003         58.603         63.546           38         39         40         41         42         43         44         45         46         47           Sr         Y         Zr         Nb         Mo         Tc         Ru         Rh         Pd         Agg           87.62         59.000         91.224         92.906         95.541         1981         101.07         102.91         106.42         107.87           88.900         91.224         92.906         95.541         1981         101.07         102.91         106.42         107.87           88.900         91.224         92.906         95.541         1981         101.07         102.91         106.42         107	4 Bee 20122         12 Mg 24 305 coldum         scanstum         titanium         vanadium         manganese         iron         colatit         rickel         copper         zmc           20 Ca 40.078 Strontum         21         22         23         24         25         26         27         28         29         30           Ca 40.078 Strontum         Sc         Ti         V         Cr         Mn         Fee         Co         Ni         Cu         Zn           40.078 Strontum         39         40         41         42         43         44         45         46         47         48           Sr         Y         Zr         Nb         Mo         Tc         Ru         Rh         Pd         Agg         Cd           87.62         bitelium         futelium         futelium         futelium         futelium         futelium         futelium         gddd102.07         102.91         106.42         102.97         112.41	4 Bee 20122         5 B 10.811           12 Mgg 24.305         13 Al 20           12 Mgg 24.305         13 Al 20           20         21         22         23         24         25         26         27         28         29         30         31           20         Ca 40.078         Siconstam         21         22         23         24         25         26         27         28         29         30         31           30         Ca 40.078         Siconstam         51.996         51.996         58.893         58.693         63.546         65.30         60.723           38         Sr         Y         Zr         Nb         Mo         Sc         98.933         58.693         63.546         65.30         60.723           38         Sr         Y         Zr         Nb         Mo         Tc         Ru         Rh         Pd         Ag         Cd         In           37.62         b8.996         91.224         92.906         95.94         198         101.07         102.91         106.42         107.87         112.41         114.82           57.62         b8.996         91.224         92.906         95.94	4 Be 0122 watershort         5 8         6 B C 10.811         5 8         6 B C 10.811         5 10.912         6 C 10.911           12 Mg 24 305 Colcium 20 Colcium 20 Ca 40.078         13 21         14 22         13 23         14 AI Si 24         13 25         14 26         27         28         29         30         31         32           Ca 40.078         Sc 3100 44.966         17.867         V         Crr 21         10.961         25.946         29         30         31         32           Ca 40.078         Sc 3100 31         50.942         51.966         51.906         54.938         56.845         98.903         58.693         63.546         65.396         69.723         72.61           Strondam 33         39         40         14         42         43         44         45         46         47         48         63.396         69.723         72.61           Strondam 33         39         40         41         42         43         44         45         46         47         48         49         50           Sr 57         72         85.996         96.544         101.07         102.91         106.42         107.87         112.41         114.82         118.71	4 Bee 90122         5 90122         6 B         7 B         6 C         7 B           12 Mg 24 305         13 Calcium 20         13 AI         14 Singuestic         15 AI         14 Singuestic         15 AI         14 Singuestic         15 AI         16 AI         16 B         17 B         17 B	4 Bee 30122         5 01201         6 0 12011         7 0 12011         8 0 12011         5 0 12011         6 0 12011         7 0 12001         8 0 12011         10 12011         10 12011 <td>4 Be 30122         5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5         6 7 8 5 5 5 5 5 5 5 5 5 5 5         7 5 5 5 5 5 5 5 5 5 5         8 5 5 5 5 5 5 5 5 5 5 5 5 5         9 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5</td>	4 Be 30122         5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5         6 7 8 5 5 5 5 5 5 5 5 5 5 5         7 5 5 5 5 5 5 5 5 5 5         8 5 5 5 5 5 5 5 5 5 5 5 5 5         9 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5

## Heavy Ion Therapy at LBNL(1975~1992)

- Although many proposals for medical accelerator facilities were put forth by Berkeley Lab researchers and their colleagues in the late 1980s and early 1990s, a combination of economic and social factors prevented their realization.
- The world's first dedicated carbon-ion medical facility, although inspired by the work at Berkeley Lab, was not built in California but in Japan



## How Texas Lost the World's Largest Super Collider

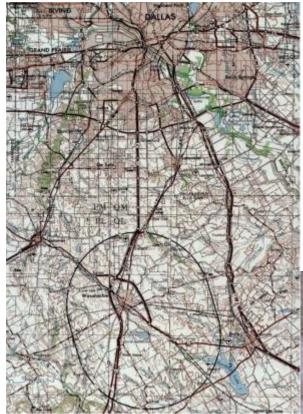


Magnablend, a chemical blending plant, bought the shell of the abandoned SSC last year. PHOTOGRAPH BY WILL GRAHAM

OCTOBER 21, 2013 | by TREVOR QUIRK | COMMENTS



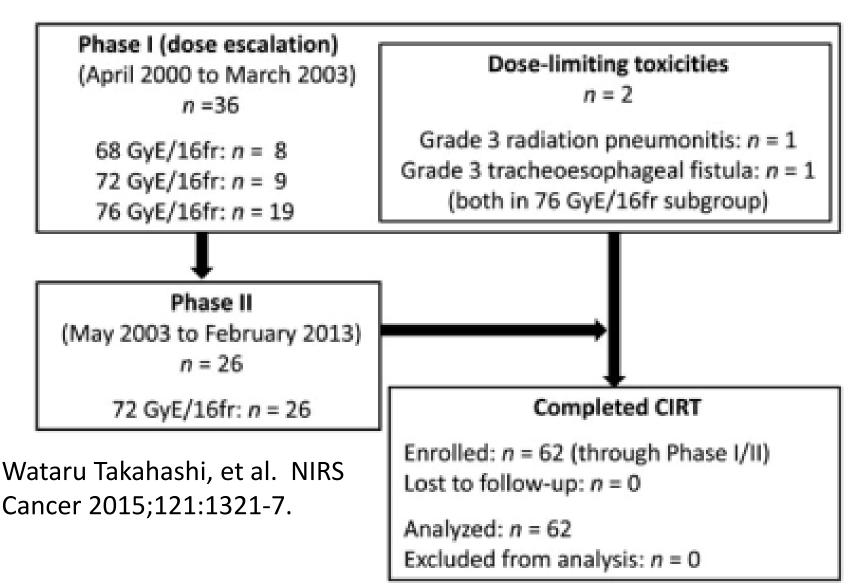
### Texas Super Collider Project (Waxahachie)



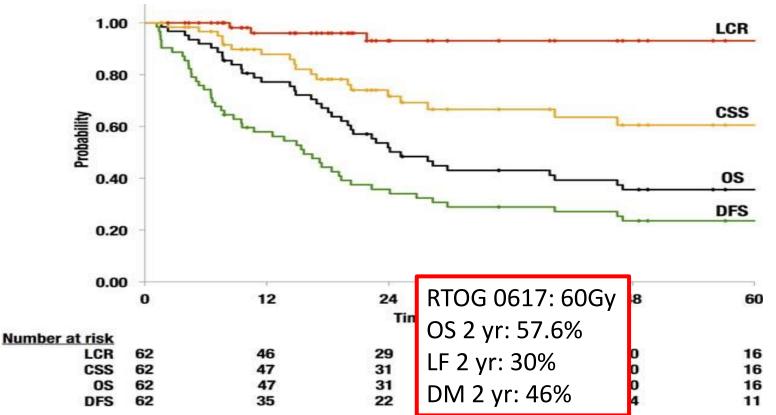
- The projected cost of construction:\$6 billion
- 16,000 acres
- 52 miles in circumference
- Annual operating budget \$600 M
- By the summer of 1993, \$2 billion and 12 miles tunnel and Congress decided to stop funding the project.



A Prospective Nonrandomized Phase I/II Study of Carbon Ion Radiotherapy in a Favorable Subset of Locally Advanced Non–Small Cell Lung Cancer (NSCLC)



A Prospective Nonrandomized Phase I/II Study of Carbon Ion Radiotherapy in a Favorable Subset of Locally Advanced Non–Small Cell Lung Cancer (NSCLC)



**Figure 3.** Overall survival (OS), local control rate (LCR), disease-free survival (DFS), and cause-specific survival (CSS) rates in 62 patients with locally advanced non-small cell lung cancer. The 2-year OS, LCR, DFS, and CSS were 51.9%, 93.1%, 35.7%, and 71.7%, respectively.

Wataru Takahashi, et al. NIRS Cancer 2015;121:1321-7.

## **TABLE 3.** Pattern of First Recurrence Sites in 62 Patients

n (%)			
0 (0)			
2 (3.2)			
1 (1.6)			
2 (3.2)			
18 (29.0)			
5 (8.1)			

Wataru Takahashi, et al. NIRS Cancer 2015;121:1321-7.

Review Article Carbon Ion The, rapy for Early-Stage Non-Small-Cell Lung Cancer

Yusuke Demizu et al.

#### BioMed Research International Volume 2014, Article ID 727962, 9 pages

Author	Institute	Year	Number of patients	Age (years)	Number of lesions	T1	T2	Total dose [Gy (RBE)]	Number of fraction	s Median FU (months)	Local control	Overall survival	Toxicity (≥grade 3)
Miyamoto et al. [21]	NIRS	2003	81	Mean 72	82	41	41	59.4-95.4	9–18	52.6	76% (5-yr)	42% (5-yr)	Lung 3.7%
Miyamoto et al. [22]	NIRS	2007	50	Mean 74.1	51	30	21	72	9	59.2	94.7% (5-yr)	50.0% (5-yr)	Skin 2%
Miyamoto et al. [23]	NIRS	2007	79	Mean 74.8	80	42	37	52.8–60	4	38.6	90% (5-yr)	45% (5-yr)	0%
Sugane et al. [24]	NIRS	2009	28	Mean 82*	2.9	12	17	52.8-72	4_9	NA	95.8% (5-yr)	30.7% (5-yr)	0%
Takahashi et al. [25]	NIRS	2014	151	Mean 73.9	151	91	60	36-50	1	45.6	79.2% (5-yr)	55.1% (5-yr)	0%
Iwata et al. [17]	HIBMC	2010	23	Median 75	23	15	8	52.8	4	$30.5^{\dagger}$	86% (3-yr)	86% (3-yr)	0%
Iwata et al. [19]	HIBMC	2013	27	Median 75 <sup>‡</sup>	27	0	27	52.8-68.4	4-10	$44^{\dagger}$	75% (4-yr) <sup>§</sup>	55% (4-yr) <sup>§</sup>	Lung 7%, skin 7% $^{\parallel}$
Fujii et al. [20]	HIBMC	2013	41	Median 76	41	26	15	52.8-70.2	4-26	39	78% (3-yr)	76% (3-yr)	Lung 5%, skin 4%

 TABLE 2: Studies of carbon ion therapy for early-stage non-small-cell lung cancer.

Gy: gray; RBE: relative biological effectiveness; FU: follow-up; NIRS: the National Institute of Radiological Sciences; yr: year; NA: not available; HIBMC: Hyogo Ion Beam Medical Center.



## International Symposium on Ion Therapy

## Emphasis on the "Heavy Ion"

## 2014 1st International Symposium on Ion Therapy

ISIT

**ISI** 

## 2015 2<sup>nd</sup> International Symposium on Ion Therapy



2016: Nov 3/4th 3rd International Symposium on Ion Therapy

## "Even if you're on the right track, you'll get run over if you just sit there"





Will Rogers