



#### Future (of )Synchrotrons for Particle Therapy

Where are we now? Where do we need to go?

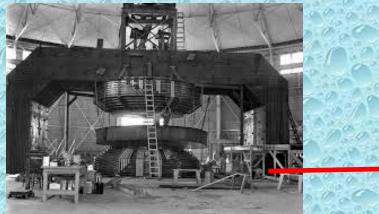
### Jay Flanz



Technical Director, Burr Proton Therapy Center Assoc. Prof. Harvard Medical School



## Berkeley: Start of Particle Therapy 184" Cyclotron to the Bevalac

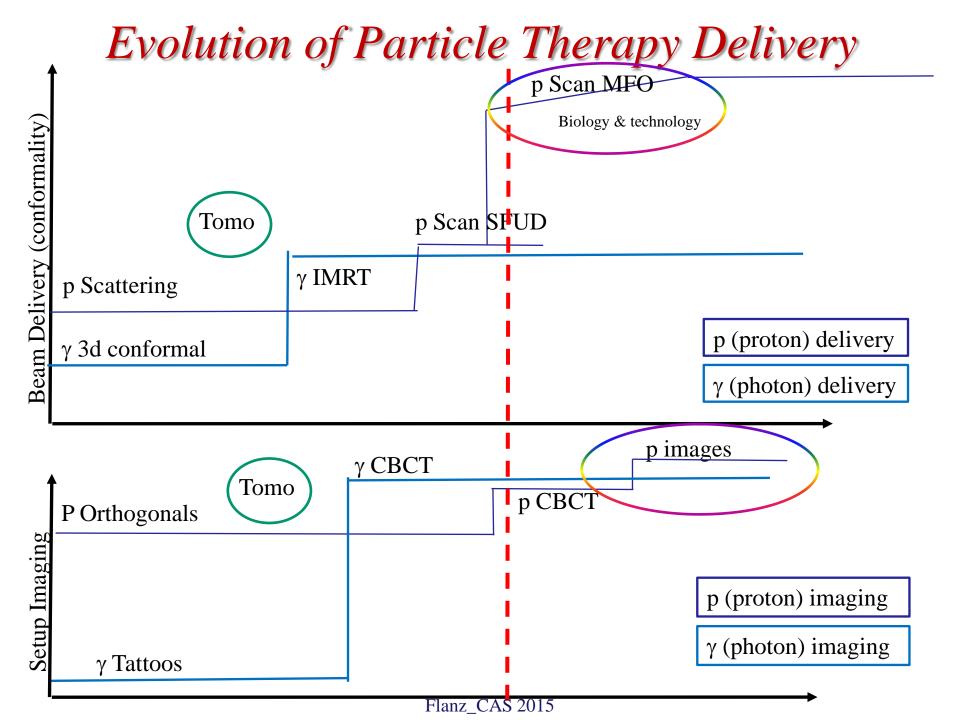












*New/Ongoing Themes in Particle Therapy:* 

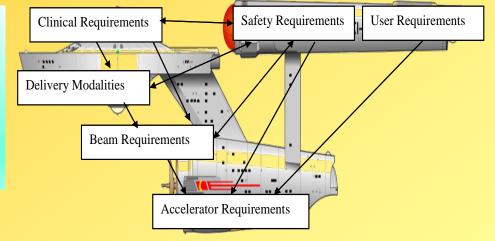
We are now in the 3<sup>rd</sup> Generation of Particle Therapy. What does that mean? Size – Cost - Quality

- 1. Beam Scanning (Pencil or Crayon) (PBS)
  - Impact on: Beam Parameters from Accelerator + Delivery
    - Scanning "type"; Beam Size; etc.
- 2. Image Guided Therapy (IGRT)
  - Impact on: Imaging; Beam Alignment
    - e.g. PROTON Radiography/Tomography
- 3. Organ Motion
  - Impact on: Beam Parameter timing; Beam Tracking; Dose Rate
- 4. Adaptive Radiotherapy
- 5. End of Range ® Proton Range vs. HU vs. Target du jour?
  - Detect Range relative to target and correct
- 6. *Field Directions*( $\theta, \varphi, \psi$ ): How to treat specific sites?
- 7. IONS: Designer Treatments with Radiobiology and multiple LETs
- 8. Increased Throughput
  - Positioning, Aligning (IGRT), Field-to-field time, Irradiation time
- 9. Lower Capital Costs **\$\$\$**

# Flow of System Requirements to the Accelerator

#### Goals of Radiotherapy

- Deliver the required dose
- Deliver that dose with the prescribed dose distribution, and
- Deliver that dose in the right place

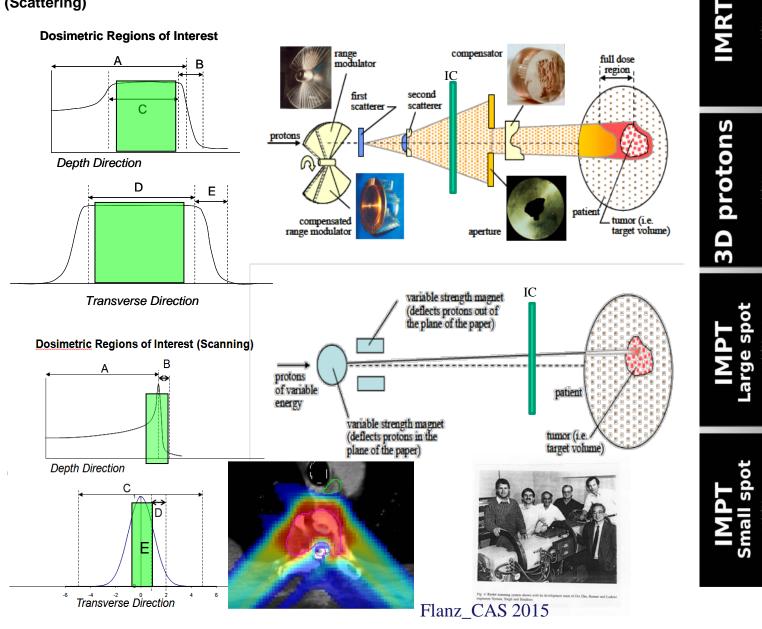


Clinical Parameter	Clinical Value	Beam Value	Accelerator Parameter
Dose Rate	1Gy/Liter/min	~100x10^9 protons/min	Beam Current
Range	32 cm (in water)	226.2 MeV	Beam Energy
Scan Beam Penumbra	80% to 20% fall off = 3.4mm	3mm sigma (e <sup>-1/2</sup> ) of a Gaussian beam)	Beam size, beam emittance

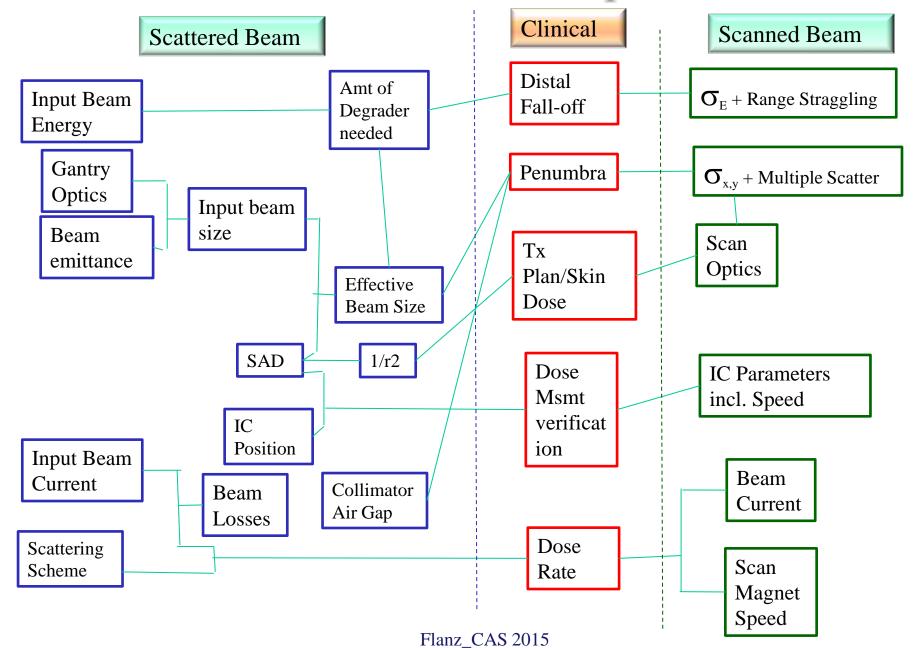
But specific 'parameter' solutions are BAD. Need System solutions for a real issue.



#### (Scattering)

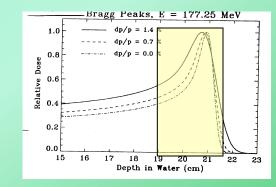


## **Clinical Parameter Dependences**



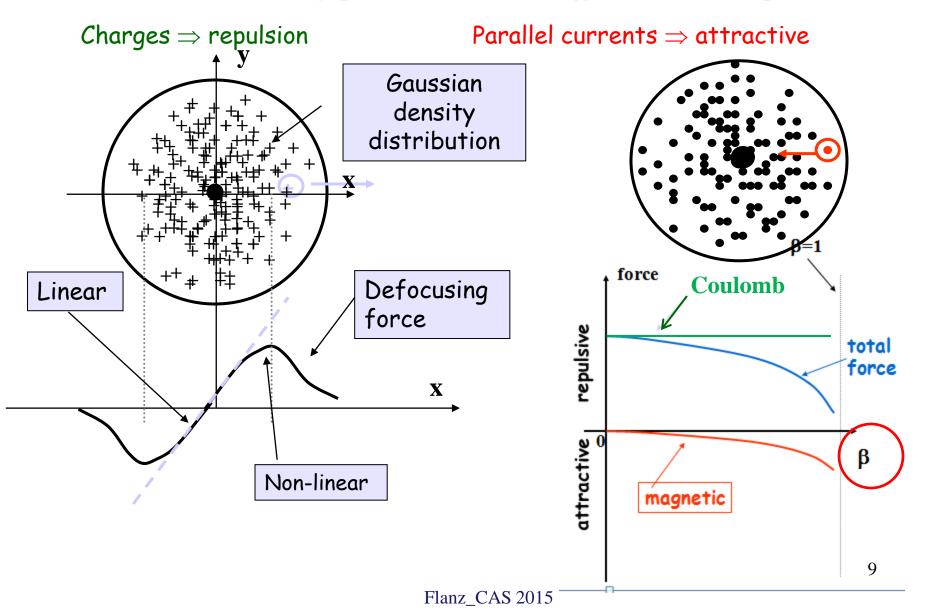
# Dose / Dose Rate (assume 1min?)

- Power = Joules/sec = Energy \* Current
  - e.g.  $\rightarrow$  150 MeV \* 1 nA = 0.15 Watts
- Dose = Joules/kg  $\equiv$  Gray (Gy)
  - Dose = (Power\* seconds) /kg
  - e.g.  $\rightarrow$  150 MeV \* 1 nA \* **60 sec** = 9 Joules
- Water  $\rightarrow$  1kg/1000cc = 1kg/liter
- Dose = 9 Joules /1kg (in a liter) = 9Gy



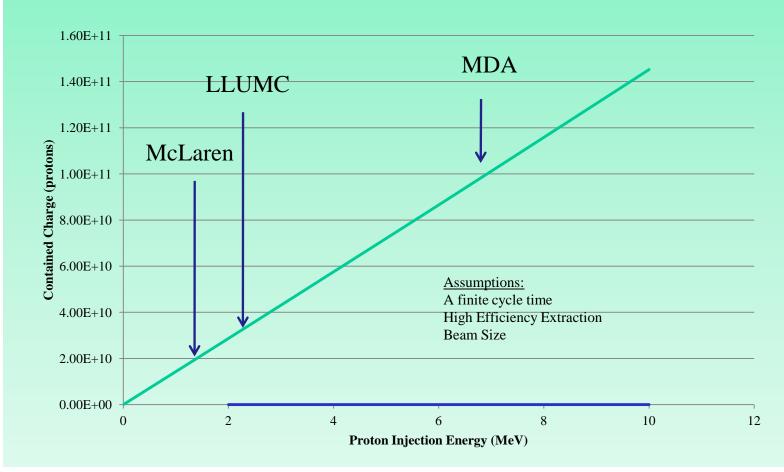
- $\rightarrow$  150 MeV, 1nA == 9 Gy in 1 liter in **1 minute**
- But not all energy goes into the target (see Bragg peak) → 3-6 Gy in 1 liter in 1 minute
- 1nA in 60 seconds  $\Rightarrow$  60 x 10<sup>-9</sup> coul  $\Rightarrow$  3.7x10<sup>11</sup> protons for 3Gy
- Therefore, for 1Gy in 1 liter we need ~ 120 GigaProtons  $(1.2x10^{11})$ 
  - (120 GP/min → ~ 0.3nA (averaged over a minute, but synchrotrons are cyclic...))

#### Accelerator Physics: Space Charge effects How many protons can be stuffed into a Ring?



#### How many protons can be stuffed in a ring? How many are needed?

**Proton Limit in Ring due to Space Charge Effects** 



Also 1Gy/min in a liter  $\rightarrow$  120GigaProtons/min  $\rightarrow$  <4Gp/cycle (2 sec cycle) 4Gp = 4x10<sup>9</sup>protons

# **Beam Current Issues**

- Current needed (standard fractionation / 1minute Tx)
  - Scattering: nAs (tens or hundreds)
  - Scanning: tenths of nAs
- Hypofractionation
  - e.g. 2 Gy/min or 10 Gy/min or more
- Fraction delivered in time < motion (1sec?)
  - e.g. <1sec  $\Rightarrow$  Earlier current numbers x 60 ?
    - $0.3nA \ge 60 = 18nA ?? NO !$
  - $2x10^{10} \Rightarrow 120 \text{Gp in } 12 \text{sec} \Rightarrow 1.5 nA$ 
    - Time limitation is dE or dx NOT nA in SCANNING
    - 1sec  $\Rightarrow$  30msec/layer Total (assume 30 layers)
  - How to change energy very fast
    - Scattered beam delivery
    - e.g. RCS (Rapid Cycling Synchrotron)
    - or What if ALL charge in only ONE fill can be used
    - OR Just a few spills, but each layer fast AND synchronized (with motion)
- \$? Cost of Charge in Ring
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- Speed/Validity of Instrumentation
  - Spot
  - Continuous
  - Recombination/Linearity
- Dose Accuracy
  - Turn off the beam
  - Beam 'reliability'
  - Beam Position

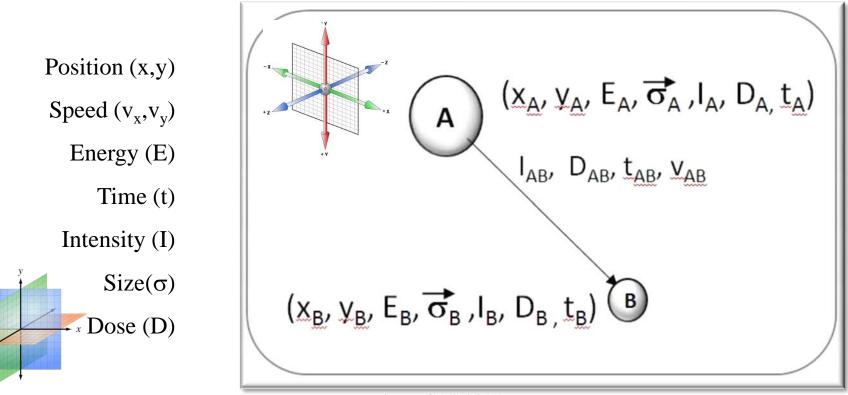
Acceleration process is cyclical

- There is a time dependence
  - It takes TIME to accelerate

# What is Particle Beam Scanning (PBS)?

The idea is to SPREAD the beam with a dose distribution that conforms to the prescription.

Beam scanning can be defined as the act of moving a charged particle beam ('relative to the target') of particular properties and perhaps changing one or more of the properties of that beam for the purpose of spreading the dose deposited by a beam throughout the target volume.



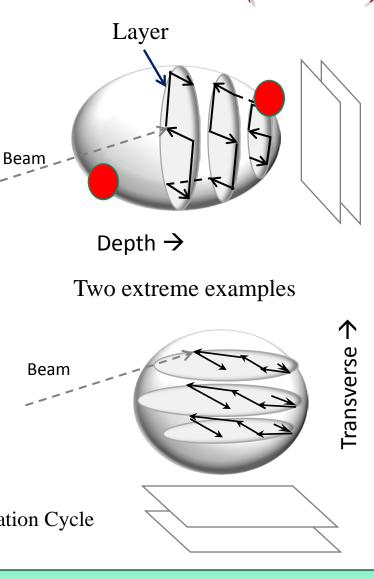
# Scanning: spread out the beam (4-5d)

- Control the beam position transversely and in depth.
- Trajectory Optimization depends upon the many factors (e.g. speed...).
- At present, the Energy (Range) Change time is longer (e.g. 5 sec to 0.1sec (PSI)) vs. milliseconds (seconds) transversely.
  - Scattering techniques cover the 3D volume either instantly (Ridge filter) or at most over about a 0.1 second time interval.
  - Normally, Scanning starts at one position and irradiates 'sequentially' taking time to reach the last 3D position. (All things being equal (in time) one could do it diff)
  - -5 sec x 25 Layers = 125 sec (2 min)
  - 0.1sec x 25 Layers = 2.5 seconds ~ Respiration Cycle
  - 0.03sec x 25 Layers = 0.75 seconds
    - Organ motion ??

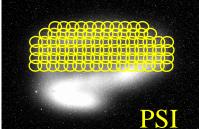


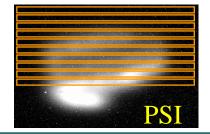
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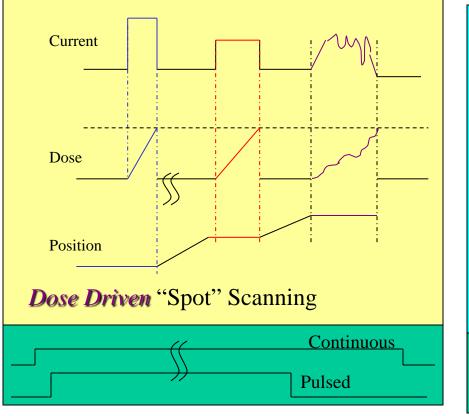
Longitudinal Conformity, Width Distal Fall-off

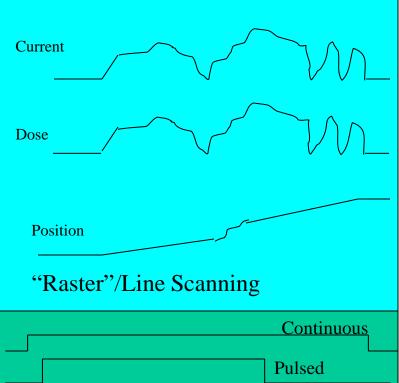


## Time Structure in Pencil Beam Scanning





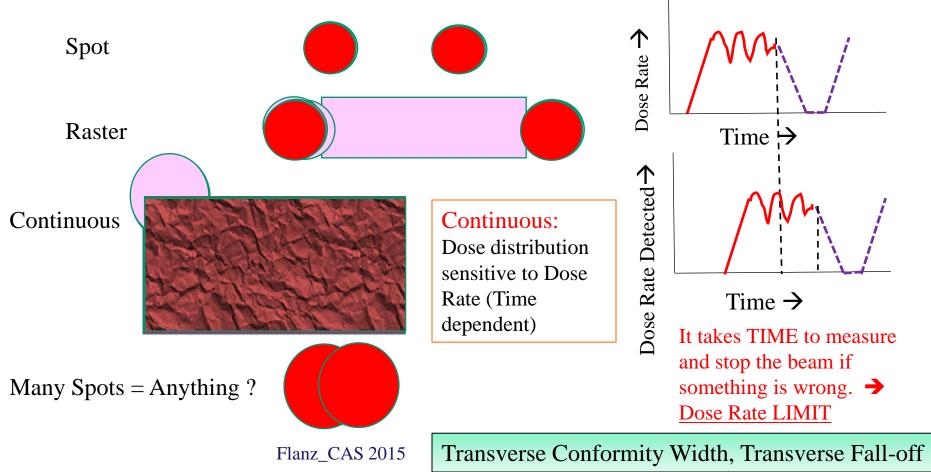




Continuous Stable/Unstable. Pulsed Short or Long

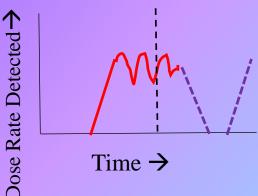
## Scanning: Timing & Transverse Dose Distribution

- <u>Dose Driven Scanning</u>: *Dose at a spot determines what to do next (not time)*.
  - Spot Scanning: Irradiate one "spot" at a time. Stop the beam while moving to the next spot. Dose at a spot determines when to move. (LCD/LED TV)
  - Raster Scanning: Irradiate one "spot" at a time (mostly). Move the beam to the next spot while the beam is on.



# Turn off time effects...

- Dose smoothness/stability/predictability
  - Contributions to turn-off delay
    - Detection
    - Calculation
    - Beam Reaction
      - Excitation (Rf KO or resonance)
      - Closed Orbit Bump?



- Uncertainty of Dose (smoothness of extraction)
  - Spot scan dose accuracy questions
    - Is beam current and turn-off time predictable?
      - » do you believe it and check after?
    - High dose region vs. Low(er) dose region (e.g. dose modulation)
      - » % tolerance depending upon relative weight of spot
      - » (MGH separate code for error tolerance/spot)
  - Continuous Position Accuracy & Dose Accuracy

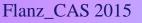
# Some numbers ...

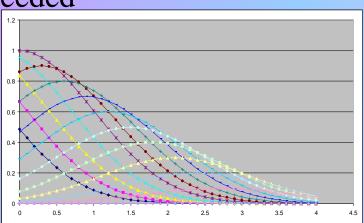
- Deliver 100 Gp for desired total dose
- $\approx 40\%$  in distal layer (if SOBP like) = 40Gp
  - Want 2% accuracy  $\Rightarrow$  within 8x10<sup>8</sup> p
  - Assume 10cm x 10cm with 5mm beam spot
    - $20x20 \text{ spots} = 400 \text{ spots} \Rightarrow 8 \times 10^8 / 400 \text{ per spot}$ 
      - $= 2 \times 10^6$  protons = TOLERANCE
  - If it takes <u>100usec</u> to respond (TOTAL) (Some places longer)
    - $2 \times 10^6$  protons / 100 usec = 3.2 na ( $1.6 \times 10^{19}$  coul/p; 1A=coul/sec)
    - Or if  $\pm 100\%$  current uncertainty  $\Rightarrow 1.6nA$  MAXIMUM current
      - vs. 0.3nA earlier for 1min Tx, vs. 1.5nA vailable from the lowest current synchrotron discussed earlier
  - Note if 1x10<sup>10</sup> per spill ⇒ ~1sec to use up protons (but MORE than one layers worth of protons AND too fast for instruments)
- If faster detection/turnoff...

# Some more numbers ....

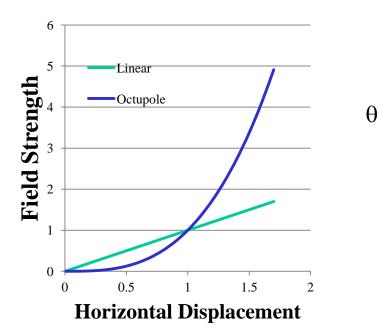
Moving beam

- 30 Hz @ 30cm
  - 33msec period or 16.5msec for 30cm
    - 18,000 mm/sec (Across meeting room in 1 second)
  - If 100usec turn off time
    - Beam will move 1.8mm (36% of 5mm beam) Too big
      - Or Maybe it is just a Penumbra increase depends how much
    - Need about 50usec (for 30Hz) (TOTAL!!)
    - If 100Hz then 17usec timing is needed
  - Change Beam Intensity?
    - ~ beam size sigma
    - $\Rightarrow$  100usec (1.8mm) for 30Hz



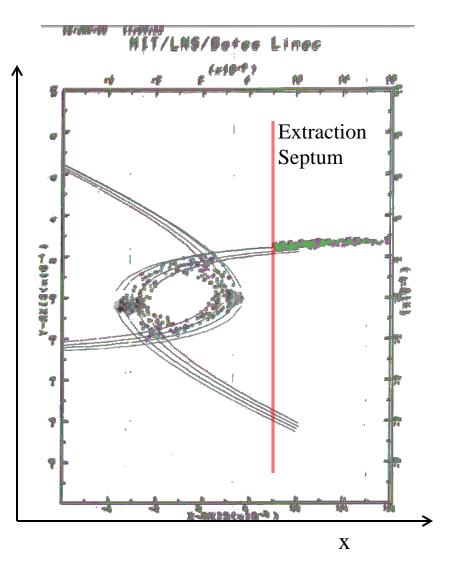


# **Resonant Extraction (one method)**



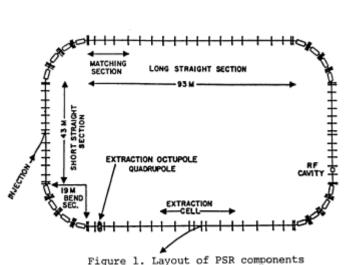
• The process is partly stochastic (uncorrected time structure is not smooth)and

• The extracted beam phase space is NOT Gaussian in the extraction plane (depending on the type of extraction).



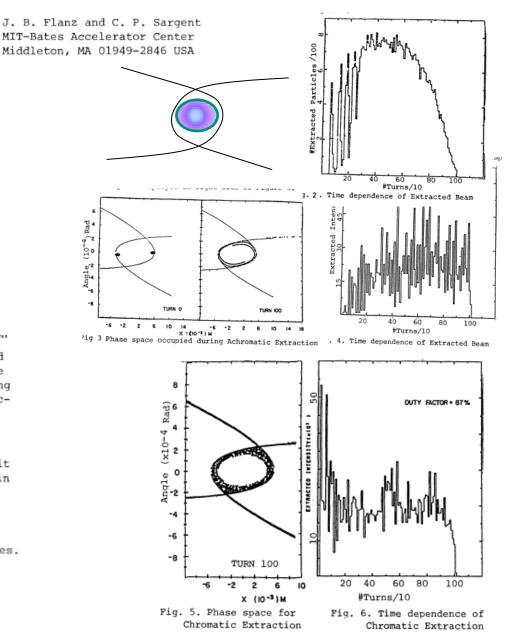
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#### SIMULATIONS OF HALF AND THIRD INTEGER RESONANT EXTRACTION FROM A ONE-GEV PULSE STRETCHER RING



Note the spiral effect and gaps evident near the fixed point vertices. This results from the tune dependence of a particle's position in phase space. The resulting output intensity is shown in Figure 4. The time structure is due to the time it takes for a particle in phase space to travel to the fixed point, or roughly 1/(2AQ) turns.

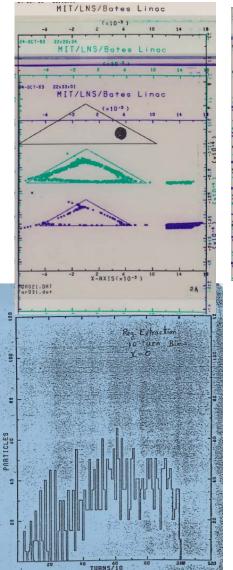
In order to optimize the resulting duty factor, it is beneficial to introduce an additional tune spread in the beam, in such a way as to not increase the nonlinearity of the extraction process. A useful method is to use the energy spread in the beam and couple it with a finite chromaticity producing a tune spread. With this technique, the output time dependence improves.

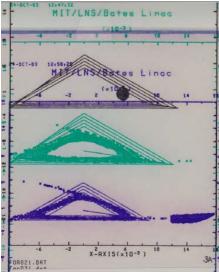


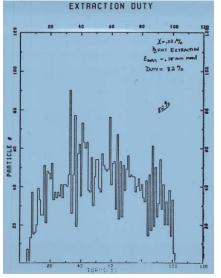
# Idiosyncrasies of Resonant Extraction

Note the spiral effect and gaps evident near the fixed point vertices. This results from the tune dependence of a particle's position in phase space. The resulting output intensity is shown in Figure 4. The time structure is due to the time it takes for a particle in phase space to travel to the fixed point, or roughly  $1/(2\Lambda Q)$  turns.

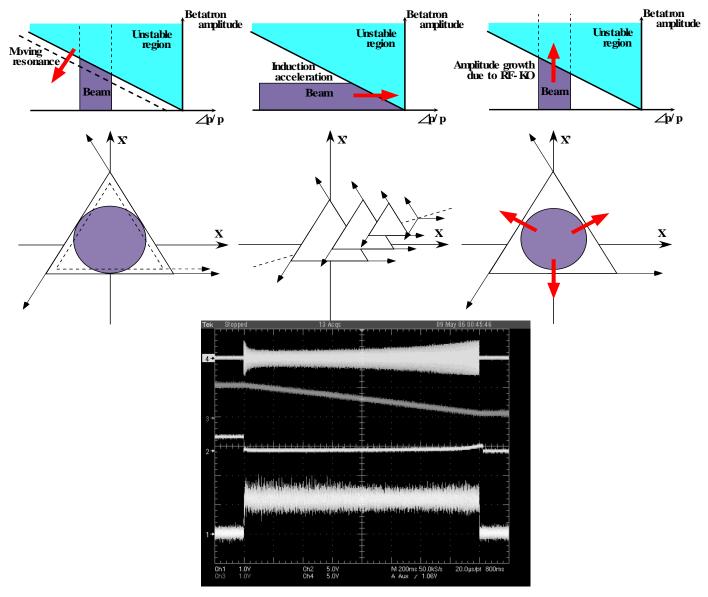
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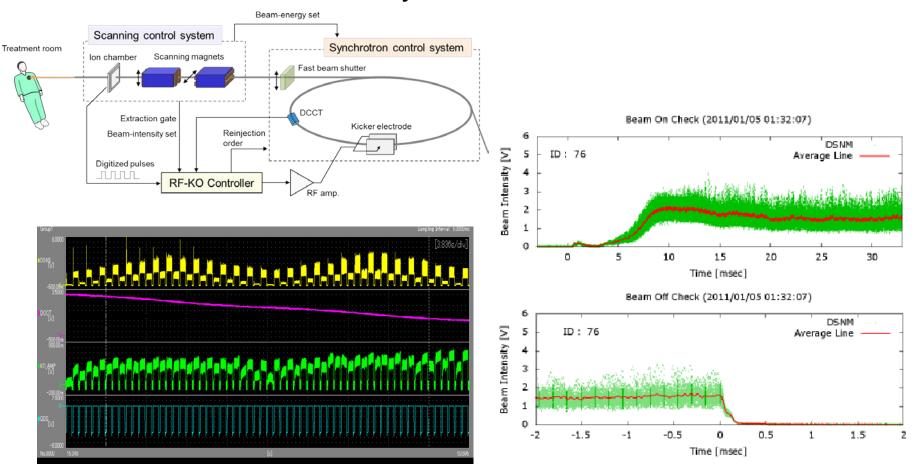




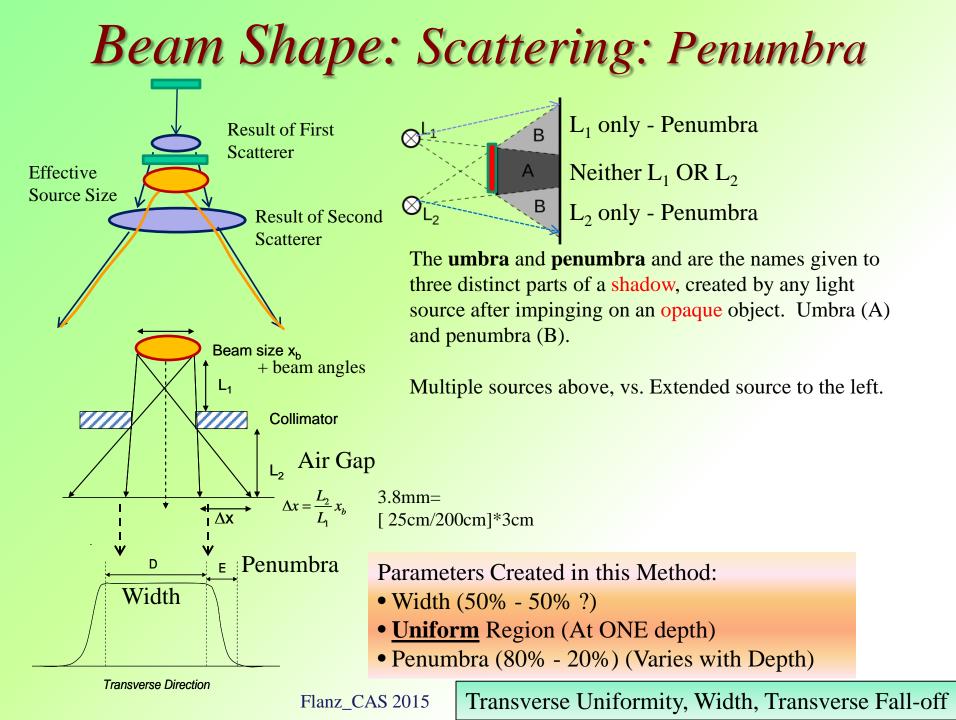
### Slow Extraction NODA

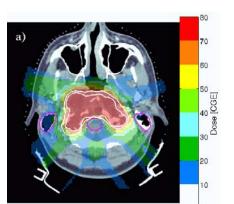


#### Response of dose rate control NODA Development of synchrotron extraction control Intensity and Beam on/off

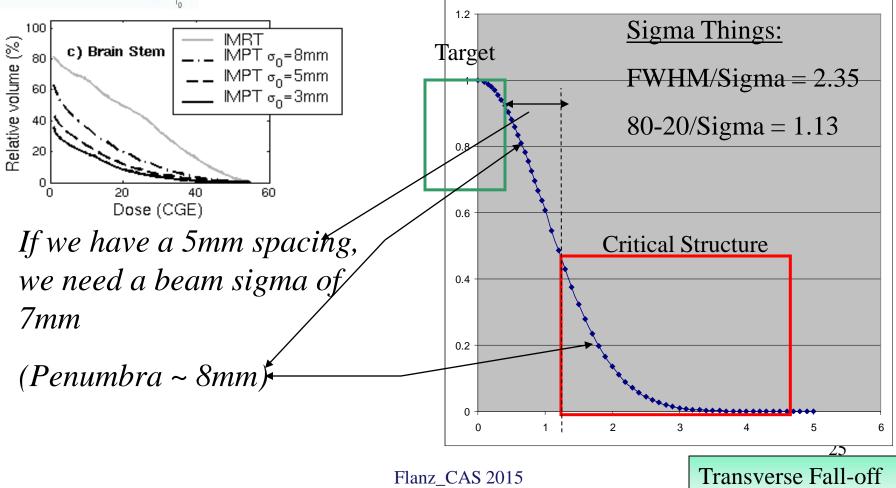


Dynamic range of modulation ~ 30 NODA Flanz\_CAS 2015

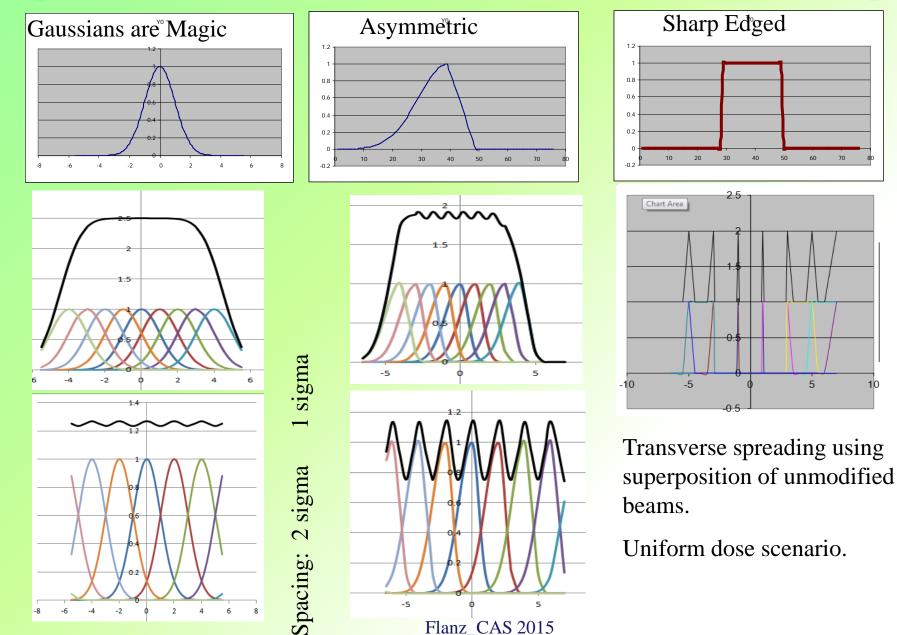




## Beam Shape: Scanning: What is the Penumbra?



## Spread out Transverse Dose with Scanned beam spots



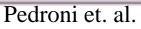
## **Beam Shape: Scanning : Penumbra Optimization**

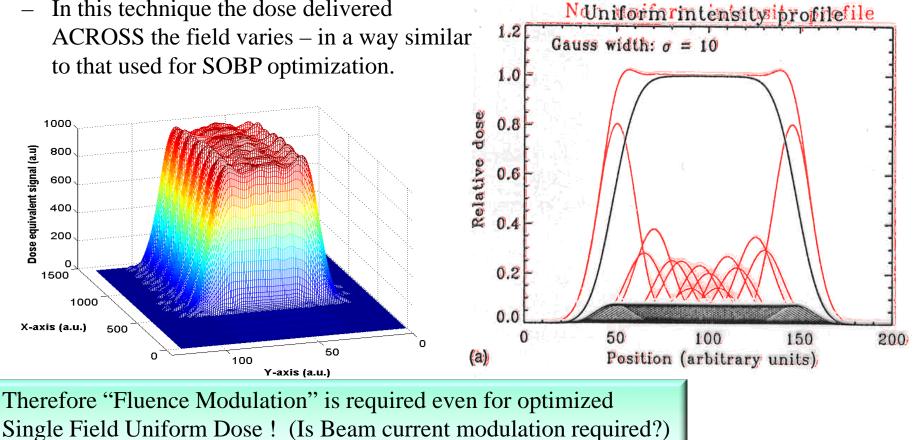
- Penumbra Optimization (Originally identified by PSI & Berkeley)
  - This results in a balance between penumbra and overall uniformity. (There will be ears.)
  - In this technique the dose delivered ACROSS the field varies – in a way similar to that used for SOBP optimization.

Dose equivalent signal (a.u)



• Apply same techniques as SOBP to sharpen the Penumbra



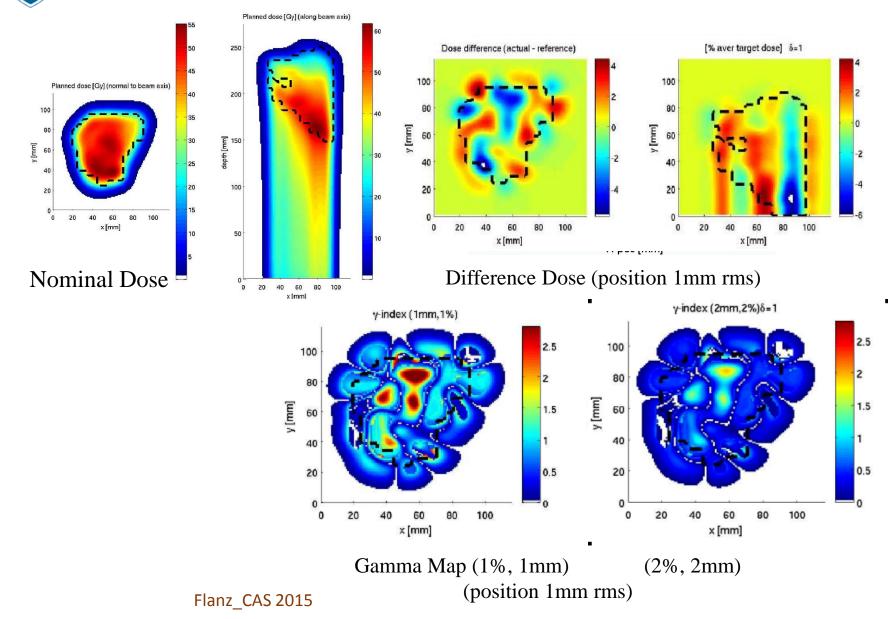


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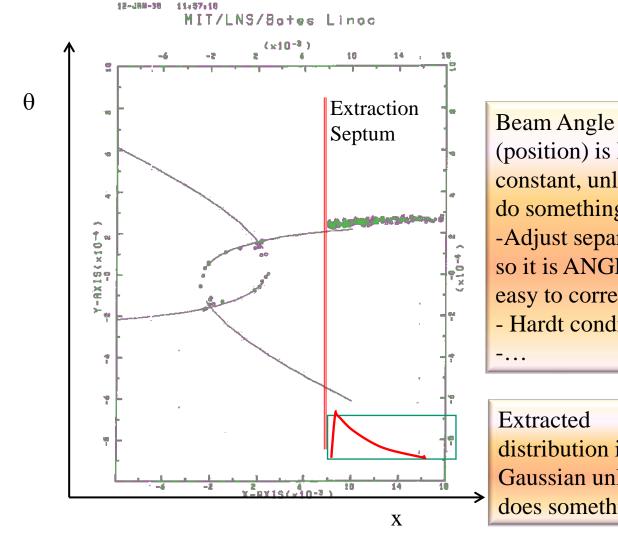
Transverse Fall-off

### **Beam Position Tolerances** Prostate, Right Lateral

MGH



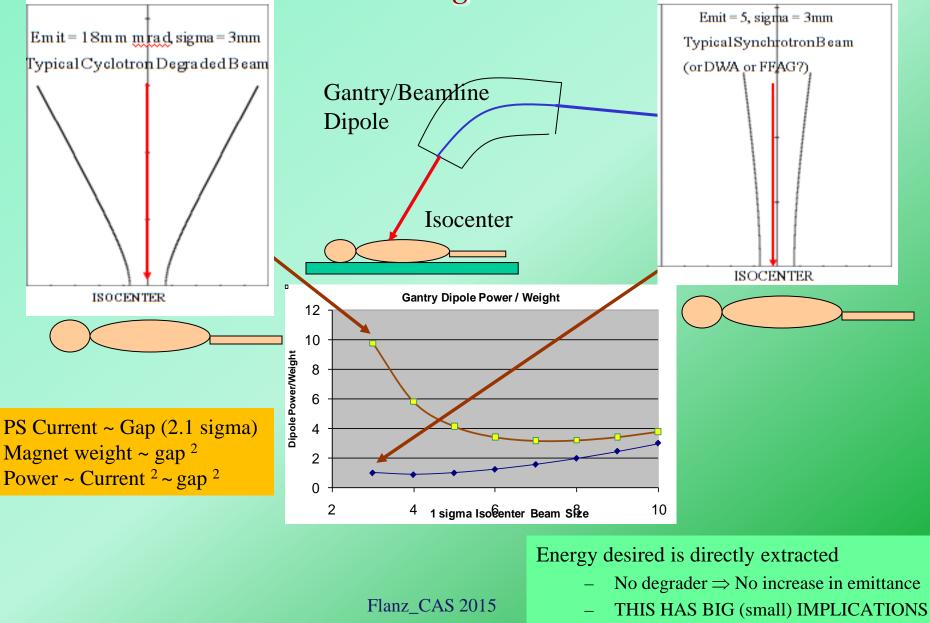
## **Beam Shape:** From a Synchrotron? Extracted Beam from Resonant Extraction (one method)



(position) is NOT constant, unless you do something. -Adjust separatrix so it is ANGLE – easy to correct. - Hardt condition

distribution is NOT Gaussian unless one does something

## Beam size Issues: Cost from the last magnet to Isocenter?



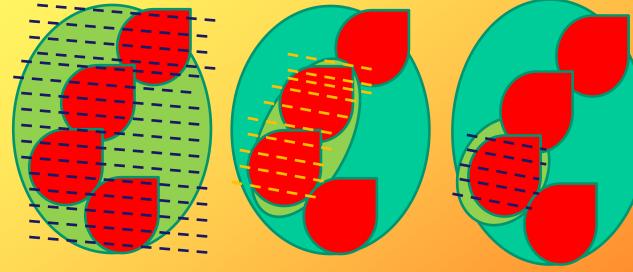
# **Organ Motion**

- Time scale of organ motion
  - Respiration seconds
  - Heart < 1 second
- Methods
  - Respiration Gating
  - Tracking
  - Fast Whole Volume Irradiation (<1 sec)
    - 1000msec/30 = 30 msec energy change
    - 1-2 % accuracy dose delivery
    - 0.1 sec/energy x 30 layers = 3 seconds: No good for this purpose? Good for overall time reduction.

## Scattering: Motion Mitigations: Nothing/Gate & ITV

NO Time Dependence of Beam Delivery

- Choosing the target to Irradiate?
  - 1. Define a ITV that is large enough to include entire motion volume and keep delivering dose until Target is uniformly irradiated.
  - 2. Define a smaller ITV and continue irradiating, until Target has passed through that region enough and is uniformly irradiated.
  - Which of the above two cases results in less healthy tissue dose?



3. Gate the beam on, when the target is in the right location.

Maybe it would be nice to see a DVH as a function of the ITV and motion effects???

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CTV - Clinical Tumor Volume GTV - Gross Tumor Volume PTV - Planning Tumor Volume ITV – Internal Tumor Volume (GTV <= CTV <= PTV<=ITV)

# **Treatment Beam Time Contributions** Longer Pulse Extraction: Synchrotron

 $T_{E'}$ 

Tcycle

Time to Inject: T<sub>1</sub>

more particles are needed or

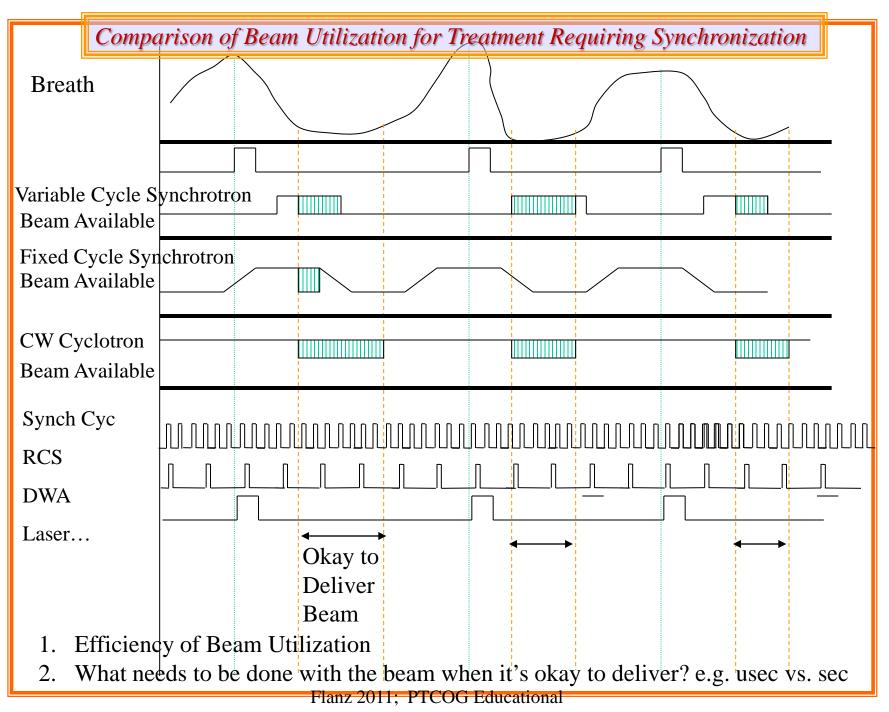
- Time to Accelerate: T<sub>En</sub>
- Time needed to wait until the patient is <u>ready</u> for particles (e.g. gating):  $T_W$

V = L dI/dt?Limit?

 $T_d$ 

- Time needed to extract particles: T<sub>b</sub> change energy
  - Instrumentation will only allow a finite number of particles per unit time
- Time needed to Decelerate: T<sub>d</sub>

Additional 'cycle' times are needed if there are not enough protons in the ring to deliver the required dose at a given range.



# On-line motion management Hitachi @ Hokkaido

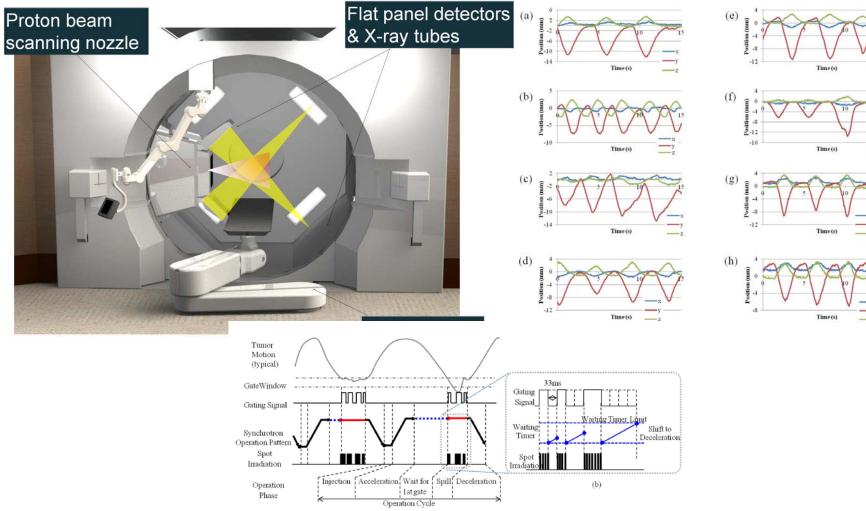


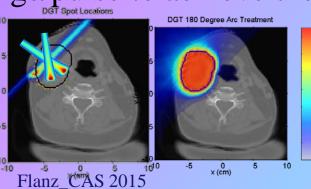
Figure 5. Diagram of the (a) synchrotron operation and (b) beam waiting function. The operation cycle of the synchrotron varies approximately from 2 to 7 s. The flat top length which consists of wait for the first gate and extraction time has a maximum of 5 s. During extraction, beam waiting function enables to irradiate proton beam to the multiple gates per operation cycle. doi:10.1371/journal.pone.0094971.g005

(a)

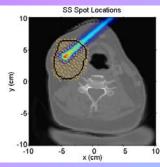
# Short Pulse beam timing?

No organ motion considerations here.

- Accelerator Timing is very important when considering SCANNING beam delivery
- For example
  - 30cm x 30cm with a 10mm beam  $\rightarrow$  1000 spots/layer
  - For 30 layers  $\rightarrow$  30,000 spots
  - 30Hz delivery  $\rightarrow$  1,000 seconds/irradiation (16.7 min!)
  - AND THIS ASSUMES 1 PULSE/Spot
  - Try 3 pulses/spot  $\rightarrow$  3,000 sec (50min)
  - Therefore to reduce to 1 min, need  $50 \times 30$ Hz = 1500Hz
- IBA, for example, has chosen 1kHz (*2x pulse/spot*) reprate for their synchro-cyclotron with multiple pulses at successively reduced charge/pulse to achieve the desired dose accuracy
- OR Use DISTAL-Edge Tracking<sup>§</sup> •

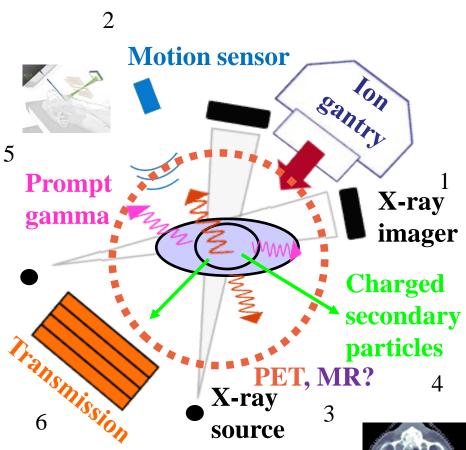


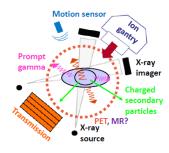
30 20

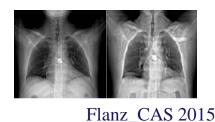


# **Implications of Imaging** ?

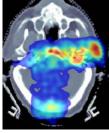
- 1. On-line: Adapt Position
  - Timing (on/off)
- 2. On-line: Adapt Position
  - Timing (on/off)
- 3. In-beam maybe:
  - Beam on/off fast
- 4. n/a
- 5. Low background;
- 6. Fast energy change; Low current; High energy

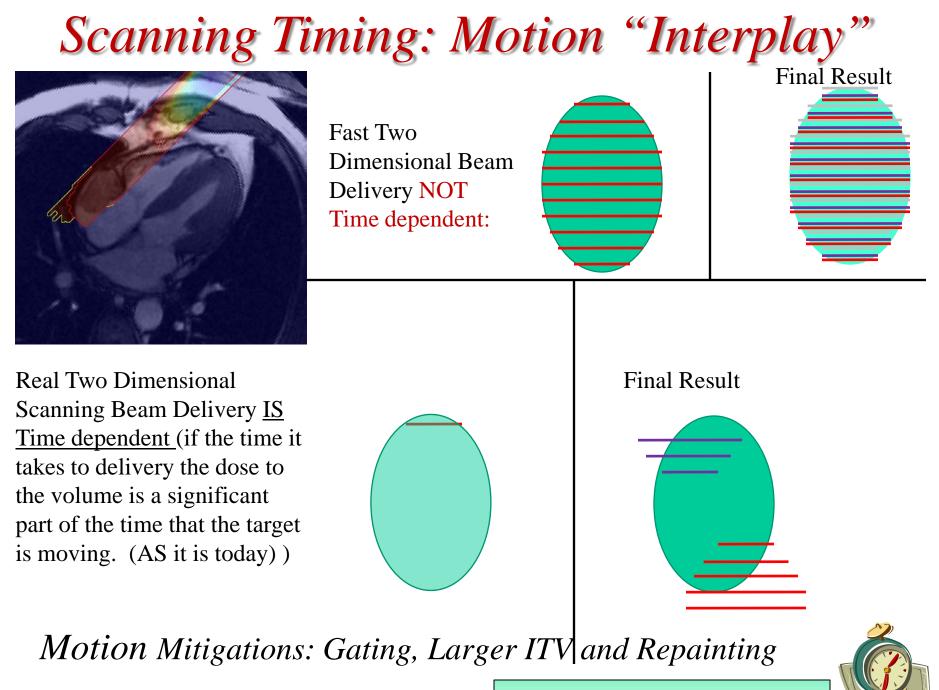






Parodi, CAS 2015





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Transverse Conformity;Width

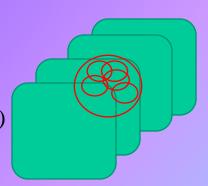
## Motion Timeframe

- Breathing motion (<u>rigid body approximation</u>)
  - Cycle about 2-3 seconds (without arresting respiration)
  - Motion amount from 3mm to 1cm (conservative not extreme)
  - Position Tolerance (depends on sigma) from 0.3mm to 3.0mm.
  - Therefore, for the WHOLE transverse scan:
    - Fastest Motion (Worse case): 10mm/2sec = 5 mm/sec (100?)
  - Tolerances gives the time required for irradiation (Freeze Layer(s)?)
    - Worst Case I: 0.3mm/(5mm/sec) = 0.06 sec (60 msec) (16 Hz)
    - Best Case I: 3.0 mm/ (5mm/sec) = 0.6 sec (600 msec)
  - What can be done in this timeframe (remember instruments)
- TRANSVERSE (e.g. spot scanning):
  - 10cm x 10cm; 3mm beam ~1000 spots
  - 1000 spots in 60msec = 60usec/point \*\* (vs. 50us turn off time before)
  - \*\* This includes response time of instrumentation and beam on/off (if needed)
- DEPTH:
  - Need same time frame as above if do NOT want to buy EASYTRACK®
  - e.g. 1 seconds =  $0.05 \sec^2 0$  layers which is < respiration cycle  $\therefore$  motion !!
  - Therefore we can complete one respiration phase if energy change is this fast. Otherwise we would have to go faster or follow more phases
- *Heartbeat timing; e.g. 80 beats/minute (0.75 sec/cycle)*

Position then Energy or Energy then Position or Mixed? Can we do faster than 0.1 sec??

Moving, Size Changing Density Changing

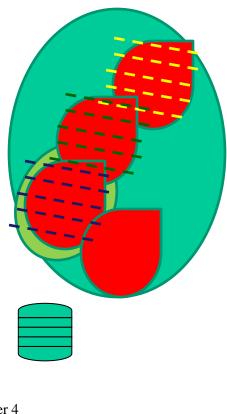
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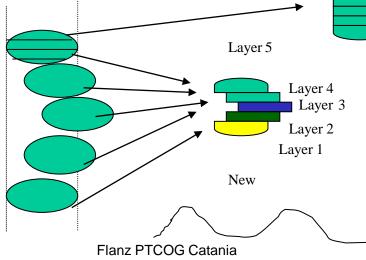
Fast or Not Moving

### Gating with EasyTrack®

- Multiple Phase Gating (*EasyTrack* ® V1)
  - Same as above (<u>Speed</u> and <u>Assumptions</u>), however prepare for irradiations during multiple phases
  - Preparation involves "<u>Known</u>" positions AND DEPTHS. Wait for target to be at those positions before delivering the beam (and do it fast).
  - <u>Time:</u> How many breathing cycles does it take to complete this irradiation? (e.g. 5 times faster in this case)



**ONE treatment plan**, just parts of it delivered at different positions. Position is phase dependent.



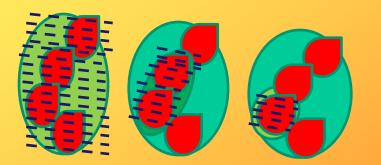
Flanz\_CAS 2015

### Motion Mitigation with Scanning: Super ® Track

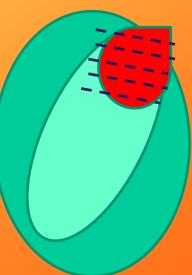
#### • Tracking of a Rigid Body:

One phase per respiration cycle <u>Assumption</u>: that during a particular phase of the cycle, the target has the same parameters Depth/Density Other moving organs in the way or not are repeatable Size and Shape Transverse Position <u>Speed of Delivery:</u> It doesn't matter if you're tracking a rigid body

<u>Time</u>: It doesn't matter if you're tracking a rigid body



NO 'effective' Time Dependence of Beam Delivery



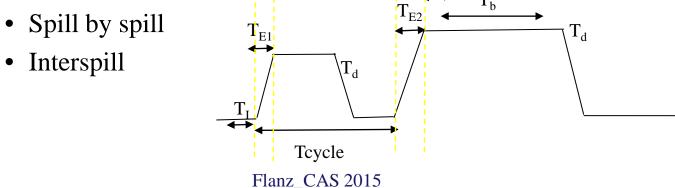
Transverse Conformity Width

## **Timing Lessons**

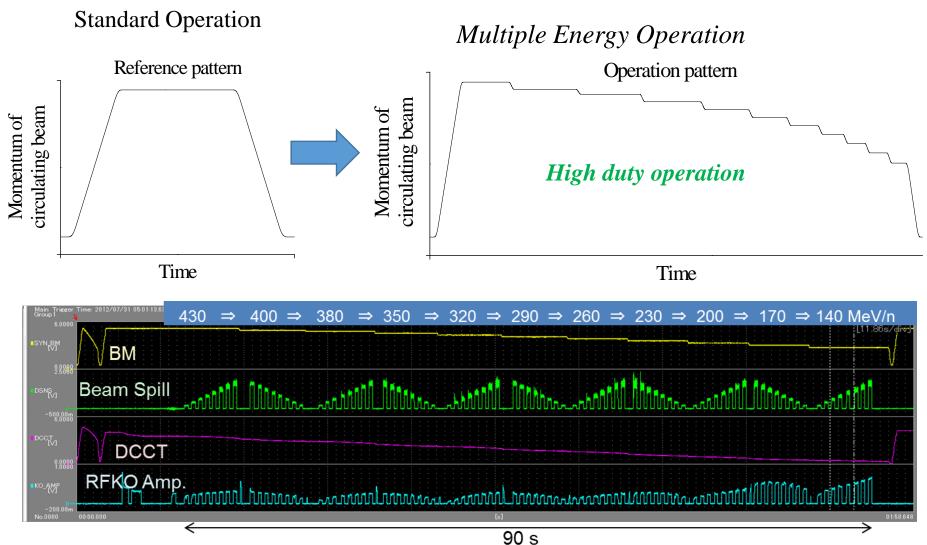
- Scattered beams are delivered in a volume almost instantaneously relative to human motion.
  - But Scattered beam distribution cannot easily be changed quickly (e.g. MLC)
- Scanned beam timing is challenging with the present technology and is a factor in delivering dose to moving targets.
  - But scanned beam potential for tracking (if there is a signal that can be used) is great.
  - The start of real-time adaptive therapy??

# Beam Range and Range Changes

- Range:
  - Therapeutic Energy only OR
  - Energy Required for Particle Imaging (Higher)
  - Lower (70 MeV? why) Is there an extraction
    dependence on Energy? (emittance/vacuum windows...)
- Scanning delivery layer by layer due to time to change layers. Much has been said about this in this talk. Reduce that time.
  - dE on same time scale as dx ? ( $e.g_{T}^{T}$  5 msec)



# Variable Energy Operation& Intensity ModulationNoda

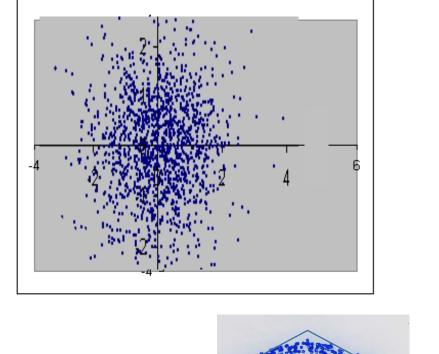


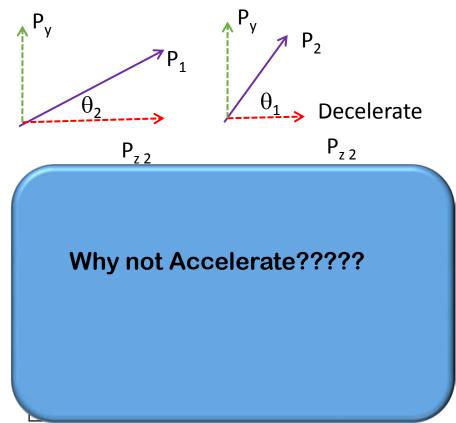
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### Decelerating a Beam

• A beam is a collection of many particles all of whose <u>longitudinal</u> and <u>transverse</u> momenta are close enough and remain more or less close to each other.

• Phase space diagram highlighting the canonical variables





# Compared to what?

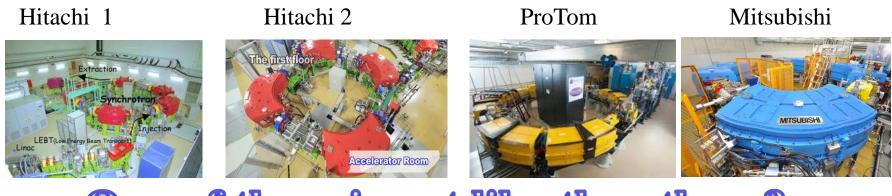
- Linac  $\cong$  \$3M
  - Equipment Only
  - Replacement (Lifetime?) = 10 years
- Proton **≅** \$100M ??
  - Equipment for 3 rooms  $\cong$  \$40 M
  - Equipment per Tx room  $\cong$  \$13 M
  - Lifetime ~ 30 years  $\Rightarrow$  \$4 M per 10 years
- ONE Room System (In an existing bldg?)
   \$25M? / what should it be?

## Small ?

- Size = Cost ???
  - Equipment costs
  - Building costs
- How to make smaller?
  - High Field
    - Special Steel
      - Harder to make
    - Superconductivity
      - Field Changing is hard (slower)
  - No magnets?
  - Reduce 'unneeded' Space
    - Define 'needed'
    - Design by "Accelerator Physics" vs. Other

## Your choice of Synchrotron Colors

#### **Proton**



### One of these is not like the others? Heavier Ions

Heidelberg

CNAO

Mitsubishi



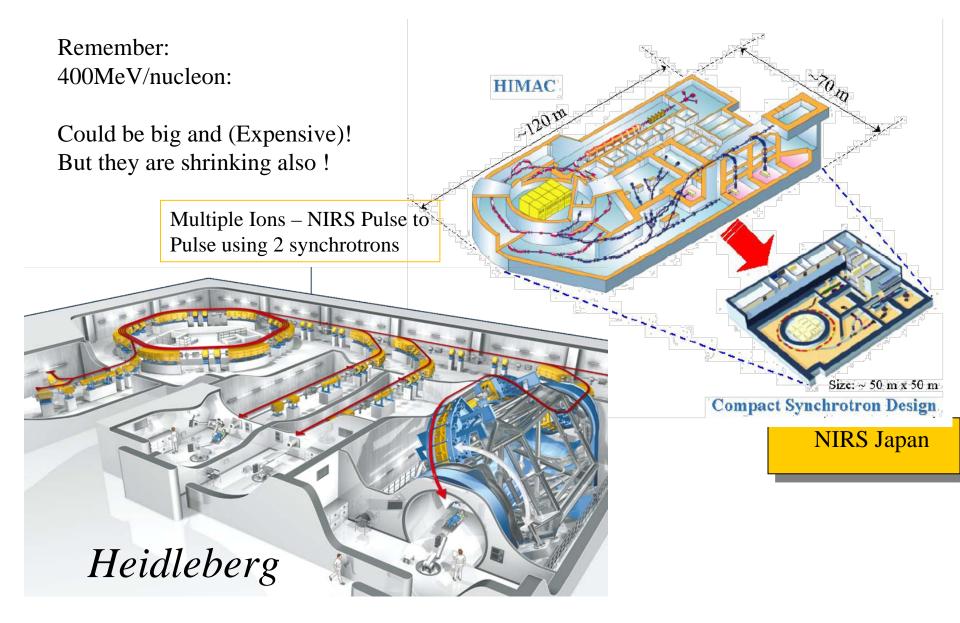




This is NOT include all synchrotrons ! I apologize for the omissions.

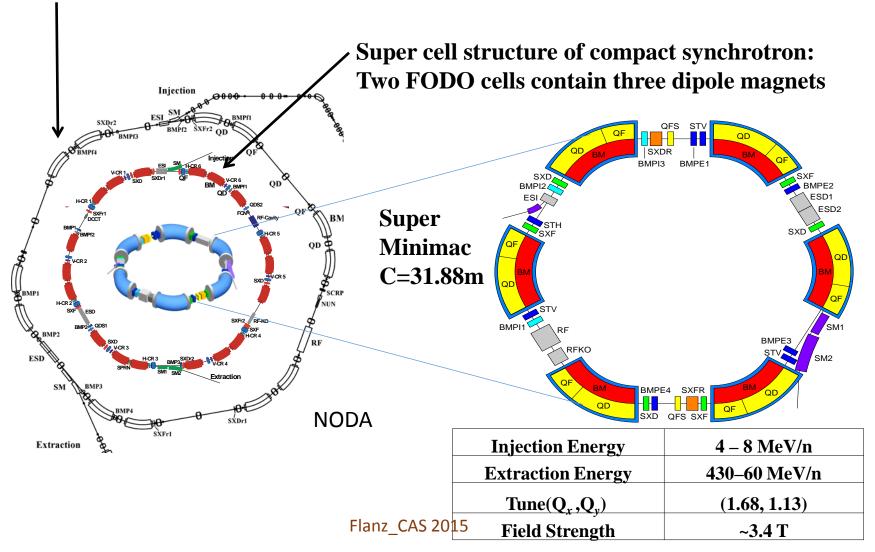
#### Flanz\_CAS 2015

### Heavy Ion Accelerators and Facilities - Conventional



### Further Reducing the HI Synchrotron Size

HIMAC Exsiting: Super cell structure of HIMAC synchrotron: Two FODO cells contain two dipole magnets C=129.6m



### <u>Scaling Down</u> Systems (Gen 3) (straightforward extensions?)



\$

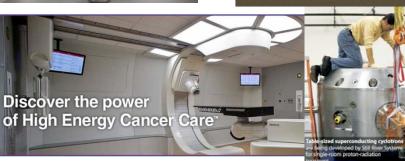




Sumitomo Axially Shorter









180° Half Width



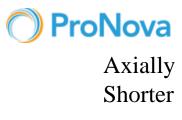










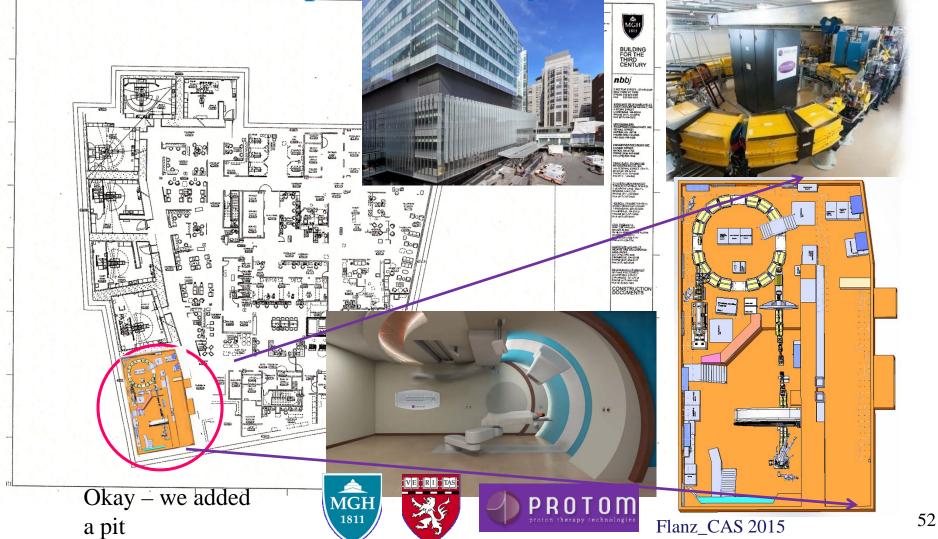






180° Half  $Width^{51}$ Flanz\_DOE 2014

### Future (?) Challenge: Install within an existing Radiotherapy Department (4<sup>th</sup> Gen?) MGH new proton facility (ADD not Replace)



## Issues for Future consideration:

- Cost:
  - Size vs. Superconducting
  - Injector energy
- Intensity
  - Injector energy vs. Cost
- Energy
  - Therapeutic only vs. Imaging vs. Low
- Energy change speed
  - Superconductivity
  - Beam storage stability
- Turn off time
  - Instrumentation detection time
  - Calculation Time
  - Extraction control parameters
- Irradiation Time (e.g. motion)
  - Full volume irradiation in ONE spill
    - In a time less than motion relevance



"Full Volume Irradiation in ONE cycle < 1 second"

"Fit in an existing Hospital Infrastructure"

# The Francis H. Burr Proton Therapy Center



### **Relationship of Themes to Beams**

		-	e/				
	Dolivory Timo		Range		Beam	Beam	lon
	Delivery Time vs. Dose Rate	Range	Change	Beam Size	Position	Shape	Species
Scanning (no							
Scanning (no motion)							
motiony							
IGRT							
Organ Motion							
Adaptive							
Radiotherapy							
End of Range							
Field Divertieve							
Field Directions							
Capital Costs							
Throughput							
Throughput							
Hypofraction							
			Consistent with	2mm – 8mm at high		Gaussian	22
Maximal Spec	Deliver <1 sec	капде	Delivery Time	Energy	10% of size	(almost)	??

# Now (P\*) vs. Future (F, FF\*) (2)

	Small	Low Cost	Fast dE	High E	Enough Q	Stable Ext	Sync Timi
Super Mimiac							
RCMS							
Hitachi							
Mitsubishi							
ProTom							
HIMAC							
CNAO							
MedAustron							
HIT							

- P = Happening Presently in clinical use
- F = Future, now working on it
- FF = Farther Future, needs development

Fast dE vs. Superconductivity (Small)

Not ALL Synchrotrons are here and I don't know all the parameters. Apologies