



# Clinical Trials for Particle Therapy in the United States

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**MD Anderson  
Cancer Center**

Making Cancer History®

No Disclosures

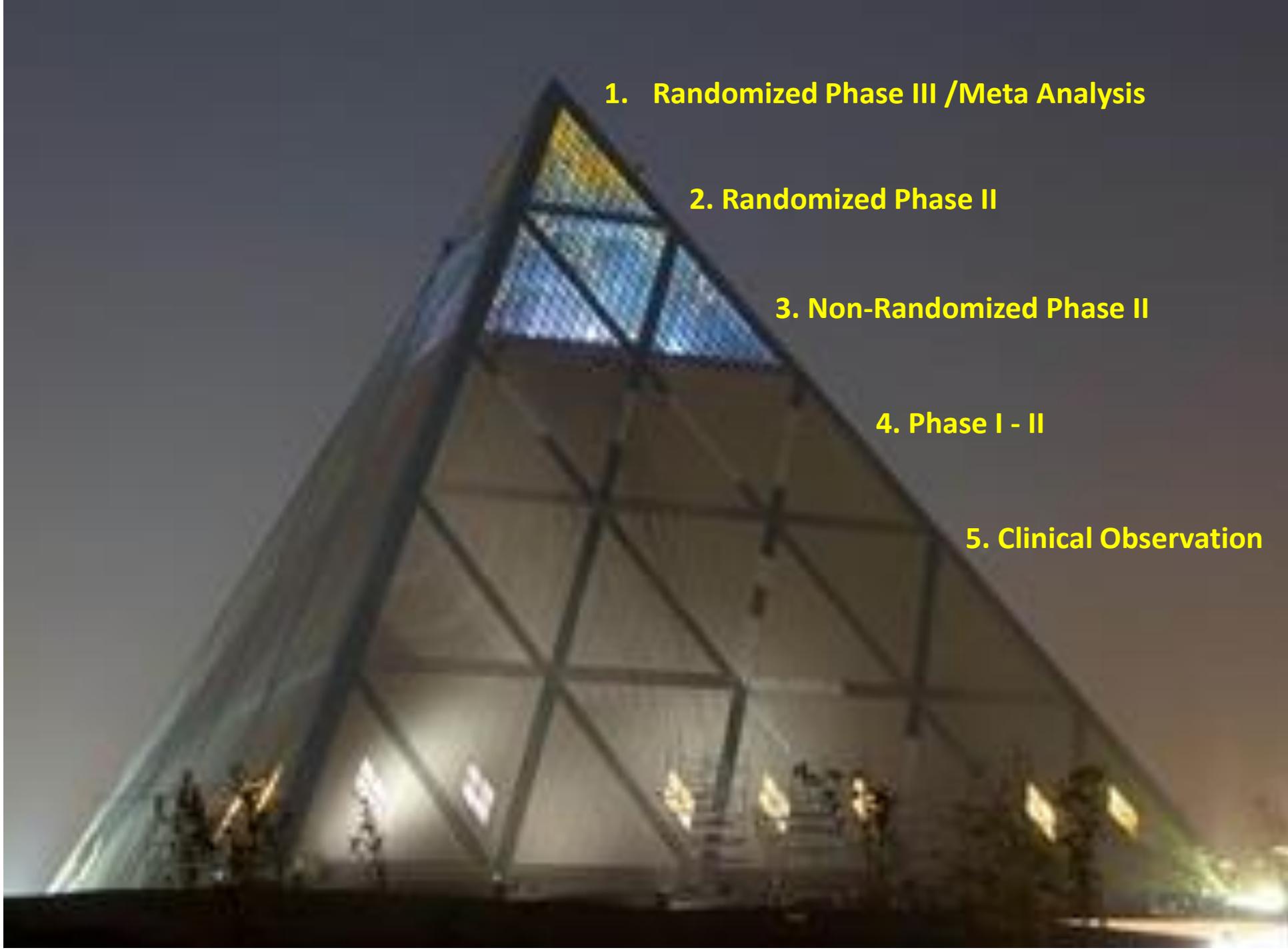
Particles Facilities in the U. S. = 17

All are proton facilities

There are no heavy ion facilities

What is the evidence that proton therapy is superior to photons?

Tumor Control  
Survival  
Toxicity



**1. Randomized Phase III /Meta Analysis**

**2. Randomized Phase II**

**3. Non-Randomized Phase II**

**4. Phase I - II**

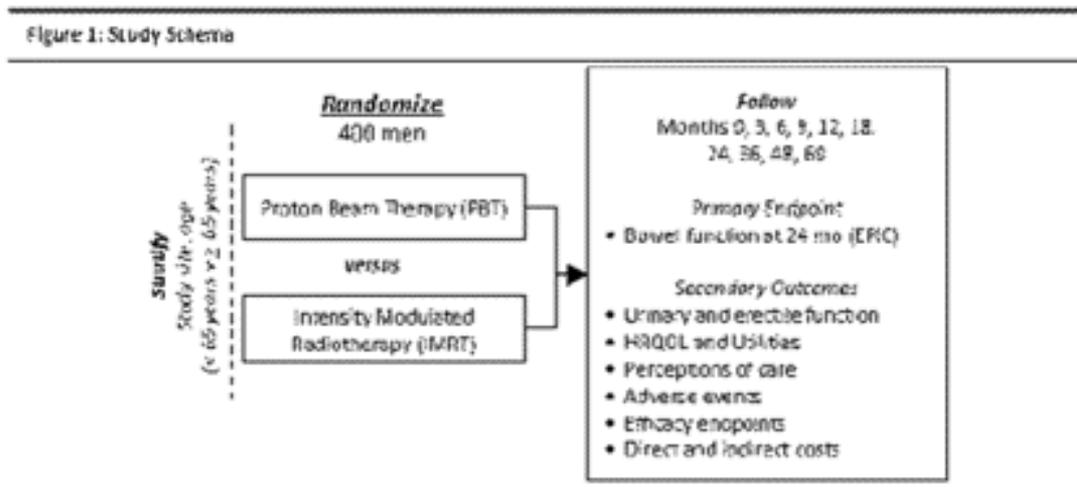
**5. Clinical Observation**

# Prostate

2013-0555

Phase III Randomized Clinical Trial of IMPT vs. IMRT for Low or Low Intermediate Risk Prostate Cancer

## Schema:



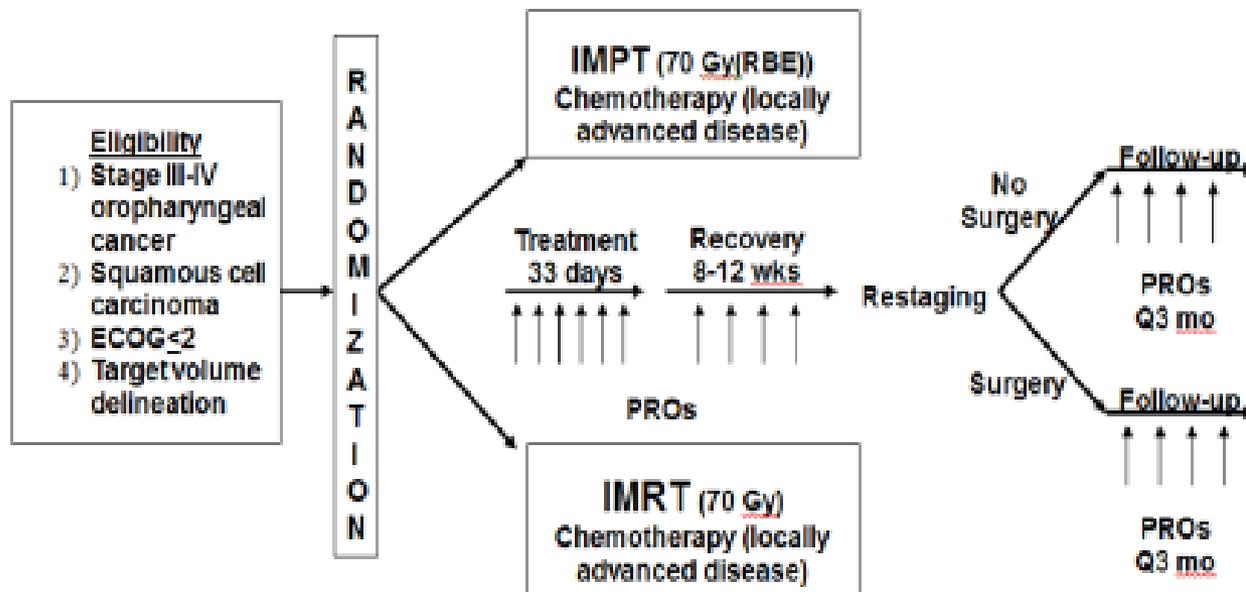
Current Accrual: 0 MDA Accrual Goal: 24 (MGH lead site)

# Oropharynx

2012-0825

Phase II/III Randomized Trial of IMPT vs. IMRT for the treatment of Oropharyngeal Cancer of the Head and Neck

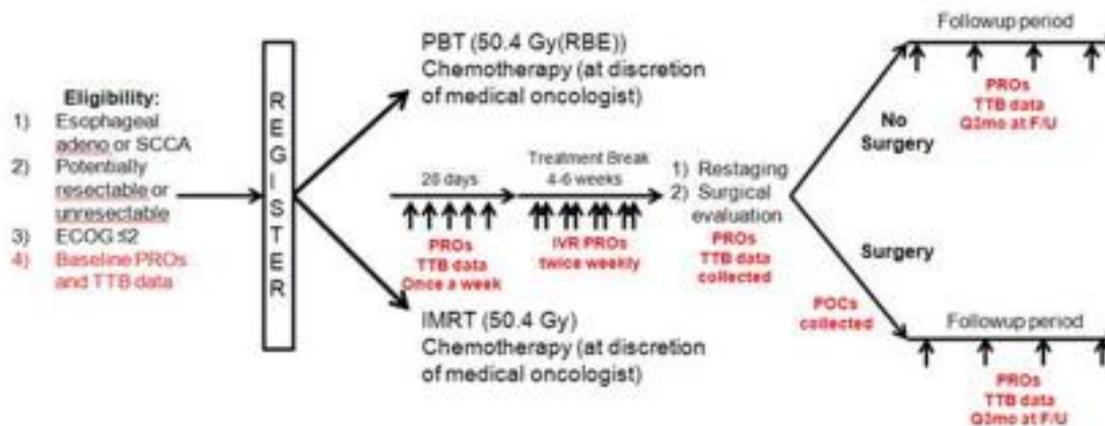
Schema:



Current Accrual: 80    Accrual Goal P2: 160    Accrual Goal P3: 200

# Esophagus

## 2011-1036 Esophageal Proton vs Photon Schema



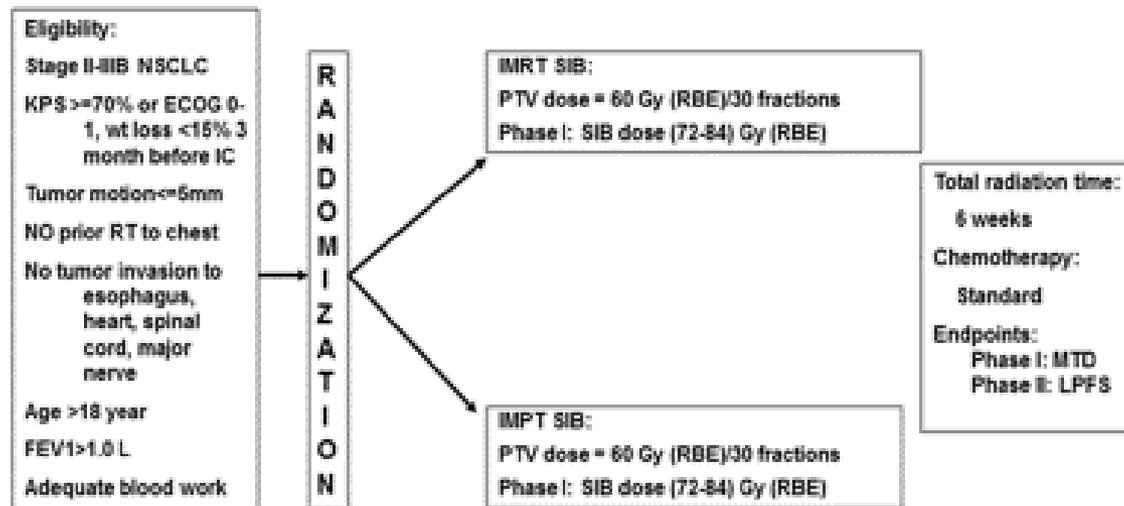
**Stratification:** Potentially resectable or unresectable, Induction chemotherapy (yes/no), early stage (stage I-II) vs stage III, Adenocarcinoma or SCCA histologies, and age ≥ 65 vs <65 years old.

**Abbreviations:** PROs = Patient Reported and Physician Reported Outcomes; TTB = Total Toxicity Burden form; IVR = Interactive Voice Response system; POCs = Postoperative Complications

# NSCLC

2011-1058 - Simultaneous integrated boost IMRT vs.  
IMPT randomized NSCLC trials

## Schema



# NSCLC

## RTOG 1308

### Phase III randomized trial photon versus proton inoperable stage II-IIIb NSCLC Schema

S T R A T I F Y	Stage		
	1. II		
	2. IIIA		
	3. IIIB		
	Histology	R	
	1. Squamous	A	Arm 1: Photon dose—70 Gy*(RBE), at 2 Gy (RBE) once daily plus platinum-based doublet chemotherapy**
	2. Non-Squamous	N	
		D	
	Concurrent	O	
	Chemotherapy	M	Arm 2: Proton dose—70 Gy (RBE), at 2 Gy (RBE) once daily plus platinum-based doublet chemotherapy**
Doublet Type	I		
1. Carboplatin/paclitaxel	Z		
2. Cisplatin/etoposide	E	Both Arms: Consolidation chemotherapy x 2 cycles required for patients who receive concurrent carboplatin and paclitaxel***	

# Breast

**Pragmatic Randomized Trial of Proton vs. Photon Therapy  
for Patients with Non-Metastatic Breast Cancer  
Receiving Comprehensive Nodal Radiation:  
A Radiotherapy Comparative Effectiveness (RADCOMP)  
Consortium Trial**

## SCHEMA

<b>S T R A T I F Y</b>	<b>Age</b> ( $<65$ vs. $\geq 65$ )  <b>Cardiovascular risk</b> (0 or 1 or 2 risk factors vs. $> 2$ risk factors*)  <b>Surgery</b> (mastectomy vs. lumpectomy)  <b>Laterality</b> (right vs. left)	<b>R A N D O M I Z E</b>	<b>Arm 1:</b> Photon dose—45.0 Gy(RBE) to 50.4 Gy(RBE) in 1.8 to 2.0 Gy(RBE) fractions with or without a tumor bed boost  <b>Arm 2:</b> Proton dose—45.0 Gy(RBE) to 50.4 Gy(RBE) in 1.8 to 2.0 Gy(RBE) fractions with or without a tumor bed boost
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\*Risk factors defined at section 4.1.2

Note: All patients will receive breast/chest wall and comprehensive nodal radiation therapy including internal mammary node treatment.

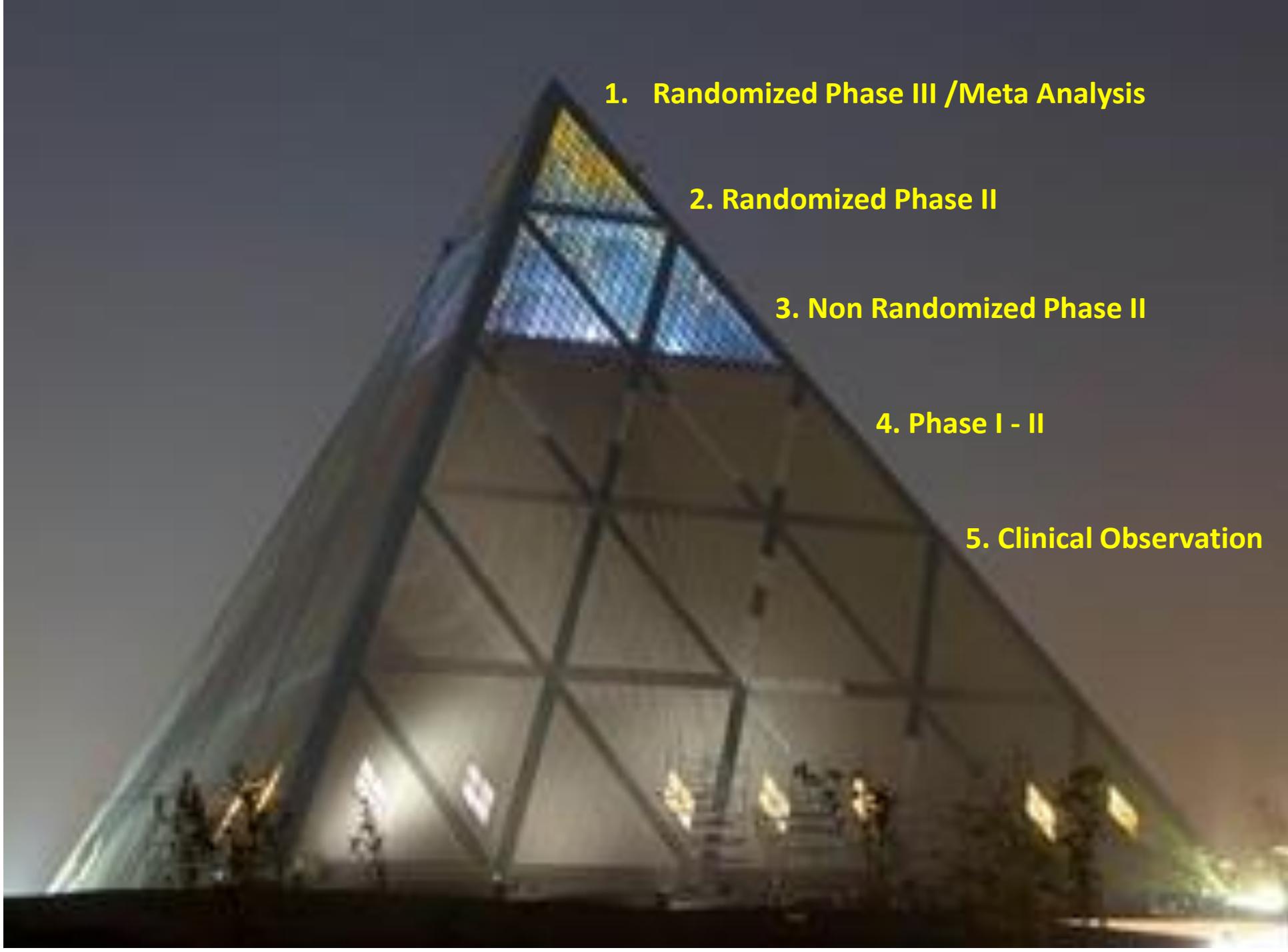
# IMPEDIMENTS LEADING TO BIAS

- Costs leading to bias in patient enrollment
  - Age
  - Insurance coverage
- Subjectivity in scoring of acute/sub acute effects
- Insufficient assessment of late effects (including second malignant neoplasms)
- Sufficient numbers of patients per arm
- Patient acceptance
- Expertise of investigators

# Results of Clinical Trials in the U. S.

It is unlikely that clinical trials for particle therapy can be conducted in the U. S. due to structural bias

Clinical trials without bias are possible in Germany and the U. K.



**1. Randomized Phase III /Meta Analysis**

**2. Randomized Phase II**

**3. Non Randomized Phase II**

**4. Phase I - II**

**5. Clinical Observation**



# Sir Michael Rawlins

Past Chair of National Institutes for  
Health and Care Excellence (NICE)

Such hierarchies are “illusory”

The totality of data is more appropriate

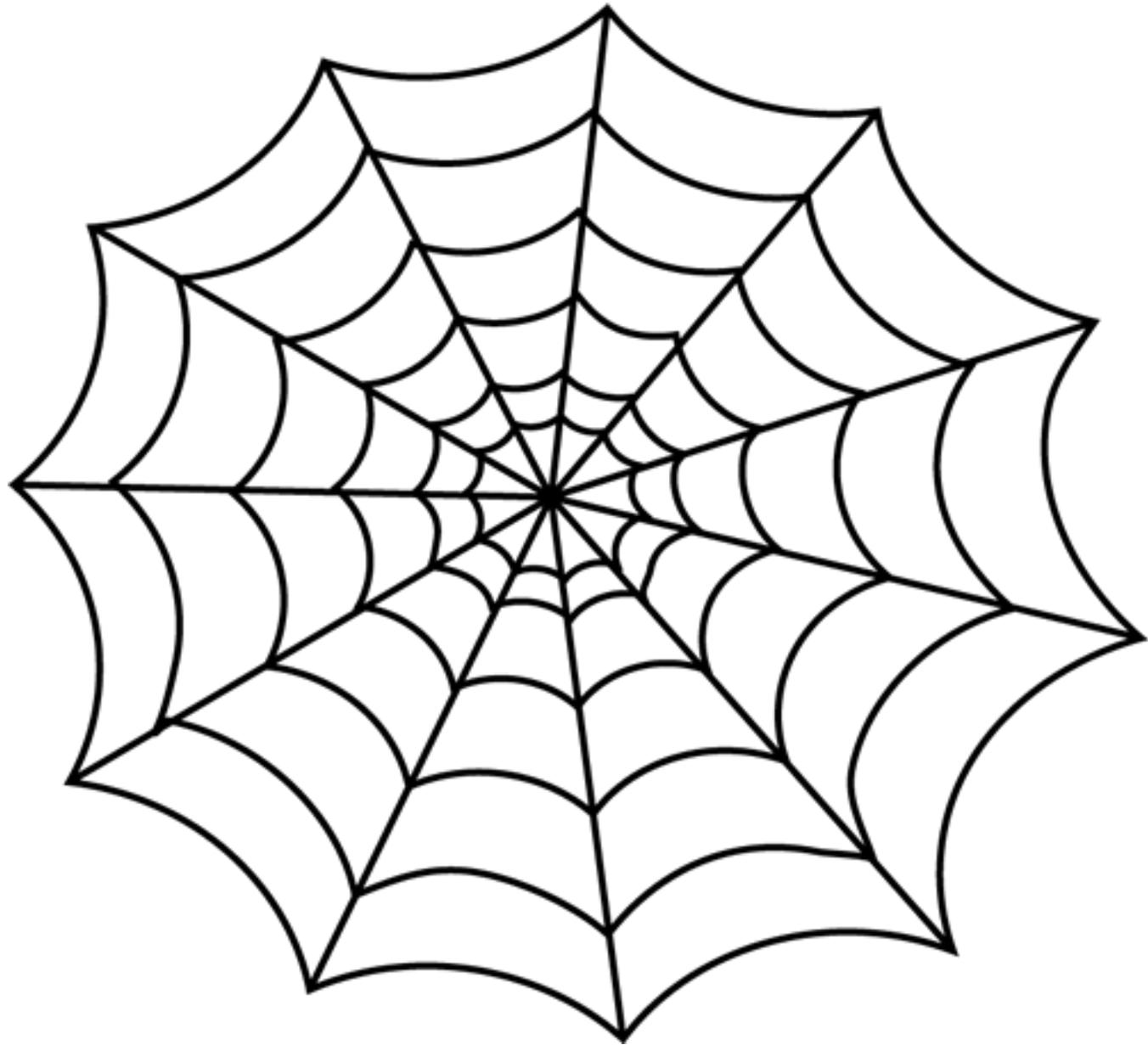


1. Randomized Phase III /Meta Analysis

2. Randomized Phase II

3. Non Random Phase II

4. Phase I - II



Particle therapy must be  
evaluated on the basis of the  
totality of available data