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Research, Innovation, and Development Process of a Radiation Therapy Device Manufacturer

Oct 15, 2021

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Sr. Mgr. Applied Research

Agenda

1. Varian History and Global Sites
2. Radiation Therapy in a Nutshell
3. High Energy X-Ray’s and Innovation Milestones
4. Innovation, Design and Development Process
5. High Energy Linear Electron Accelerators

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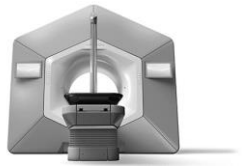
Introduction

The History of Varian – an Overview



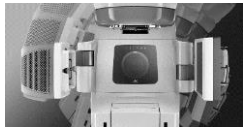
1937 — **Physics' Corner**
Invention of the Klystron in 1937 at Stanford University

1948 — **Foundation**
Varian Associates was founded

1961 — **Varian's First Accelerator**
First patient to receive radiation therapy from medical linear accelerator

1990 — ABB varian

2003



IGRT / Patient Positioning
R&D 100 award for the on-board imager

2010 — **TrueBeam**
The new digital platform of radiotherapy

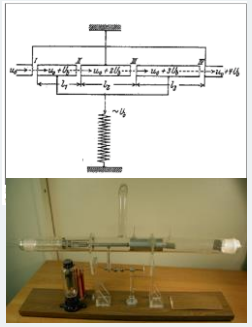
2017 — **Halcyon**
A transformation in cancer treatment delivery & management

2019

ETHOS
Online Adaptive Radiotherapy

2021 — SIEMENS Healthineers varian

1927 — varian



1946 — BBC BROWN BOVERI

Rolf Wideröe (1902 – 1996)
Studied at the Technical University Karlsruhe
Joined BBC in 1946
Professor at the Federal Insititue of Technology Zuirch (1953-1972)

1951

Betatron
First Betatron at University Clinic in Zürich

1980 — ABB

Dynaray
Switch from betatron to linac production.

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Key global sites

- Linac Manufacturing
- Linac Add-On Manufacturing
- Proton Therapy Manufacturing

10,000
employees

12
production facilities in North America, Europe, South America, and China

>70
sales and support offices around the world

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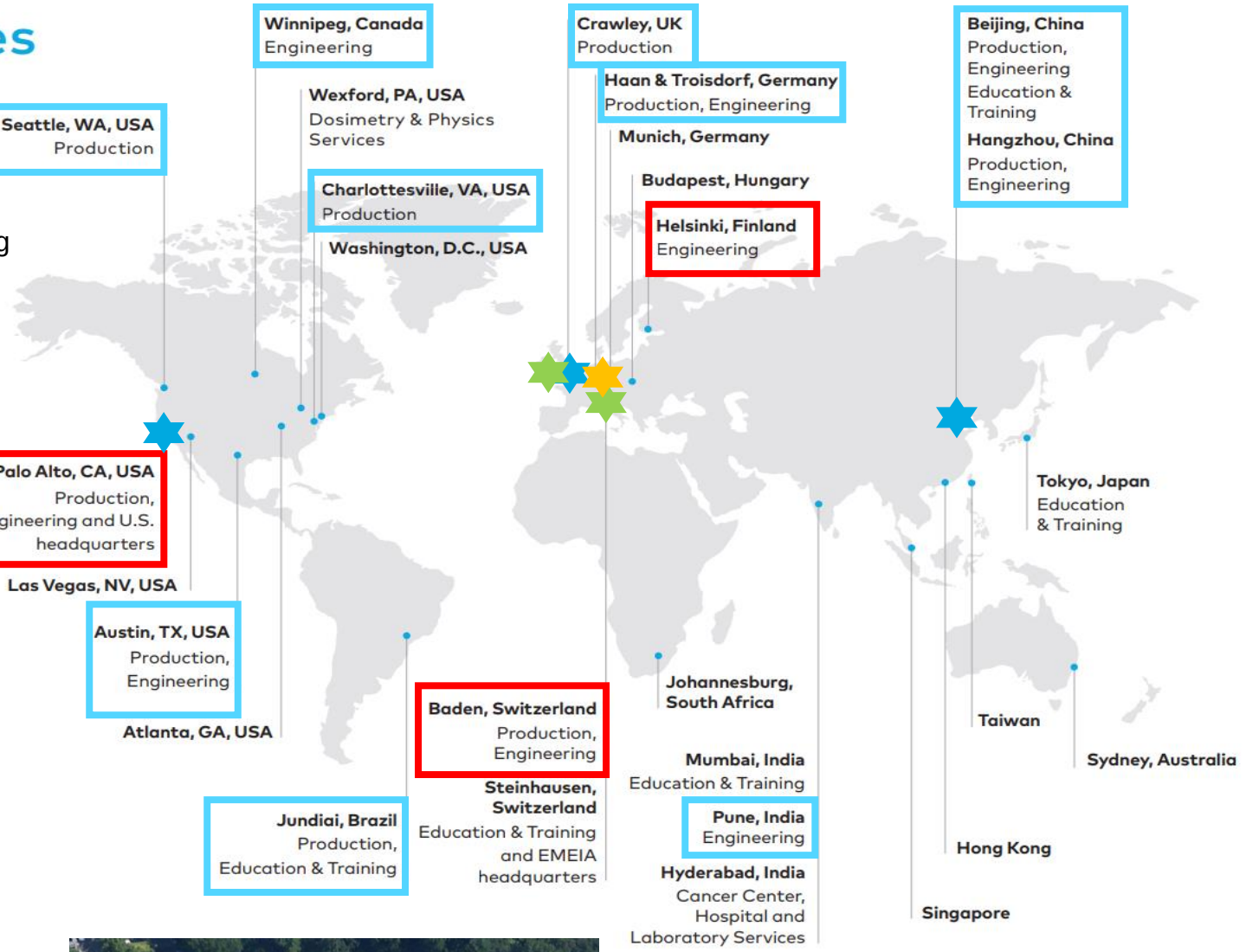
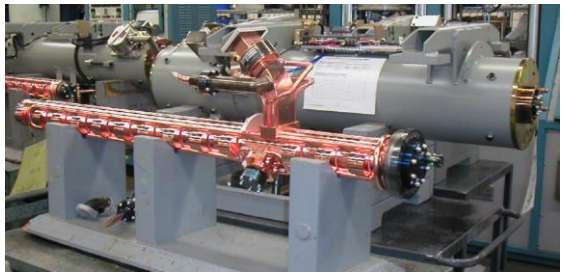
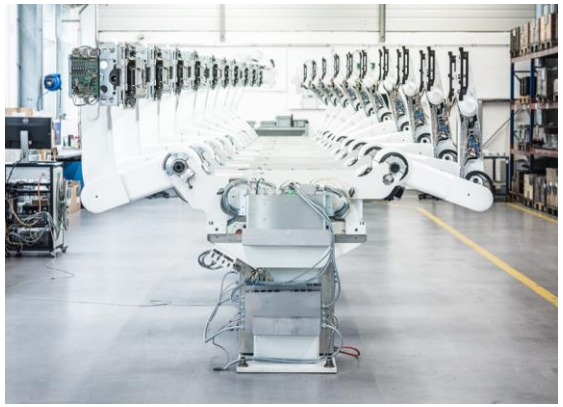
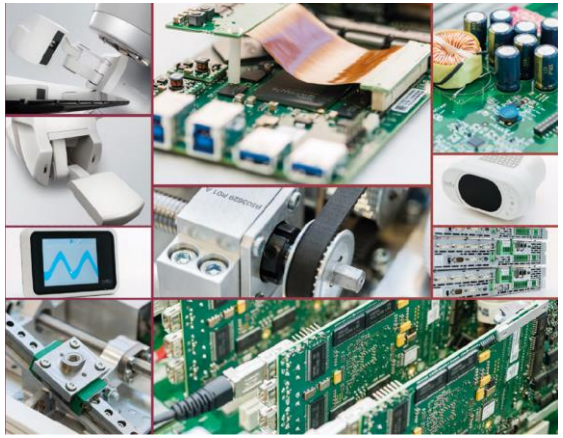


- Varian Center of Excellence for Imaging
- Mission: “Image guided Positioning and Tracking”
- Applied Research in Imaging

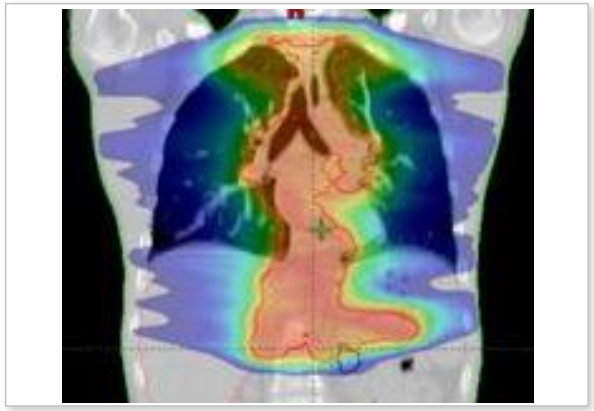


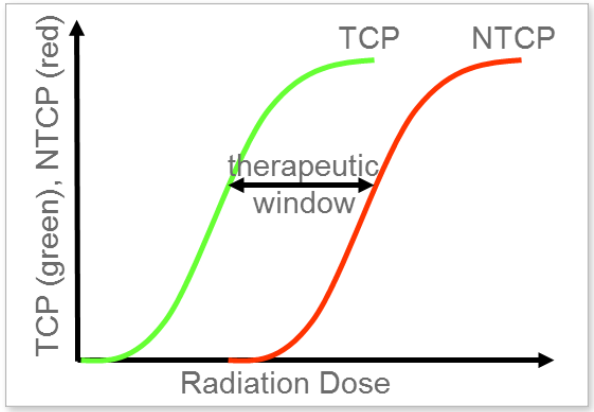


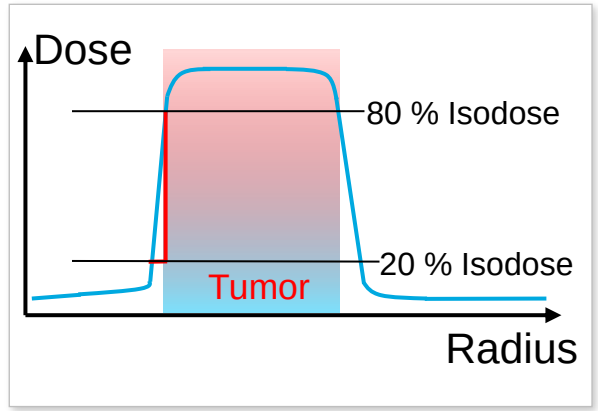


Radiation Therapy in a Nutshell

Three Important Facts to be known – with a focus on curative intent







Dose Conformity

- Focus radiation dose to tumor while sparing healthy normal tissue
- Positive effect of fractionation – up to 40 daily fractions – radiation biology
- Dose per fraction: 1.8 – 2.2 Gy, up to 90 Gy in a single fraction. Total dose range: 30 – 80 Gy
- Positive effect of escalated dose to tumor

Tumor Control Probability (TCP), Normal Tissue Complication Probability (NTCP)

- Maximize complication free tumor control
- Therapeutic Window is often small or not existing
- Geometrical accuracy (image guidance and motion management) is important
- NTCP depends on organ (serial, parallel) and volume treated – known tolerance doses

Dose Gradient

- High dose gradients to be placed accurately are often important – Imaging required
- Positive effect of high local doses and high dose gradients – single/few fractions – Dose escalation potential
- Reduction of safety margins around the tumor is often important

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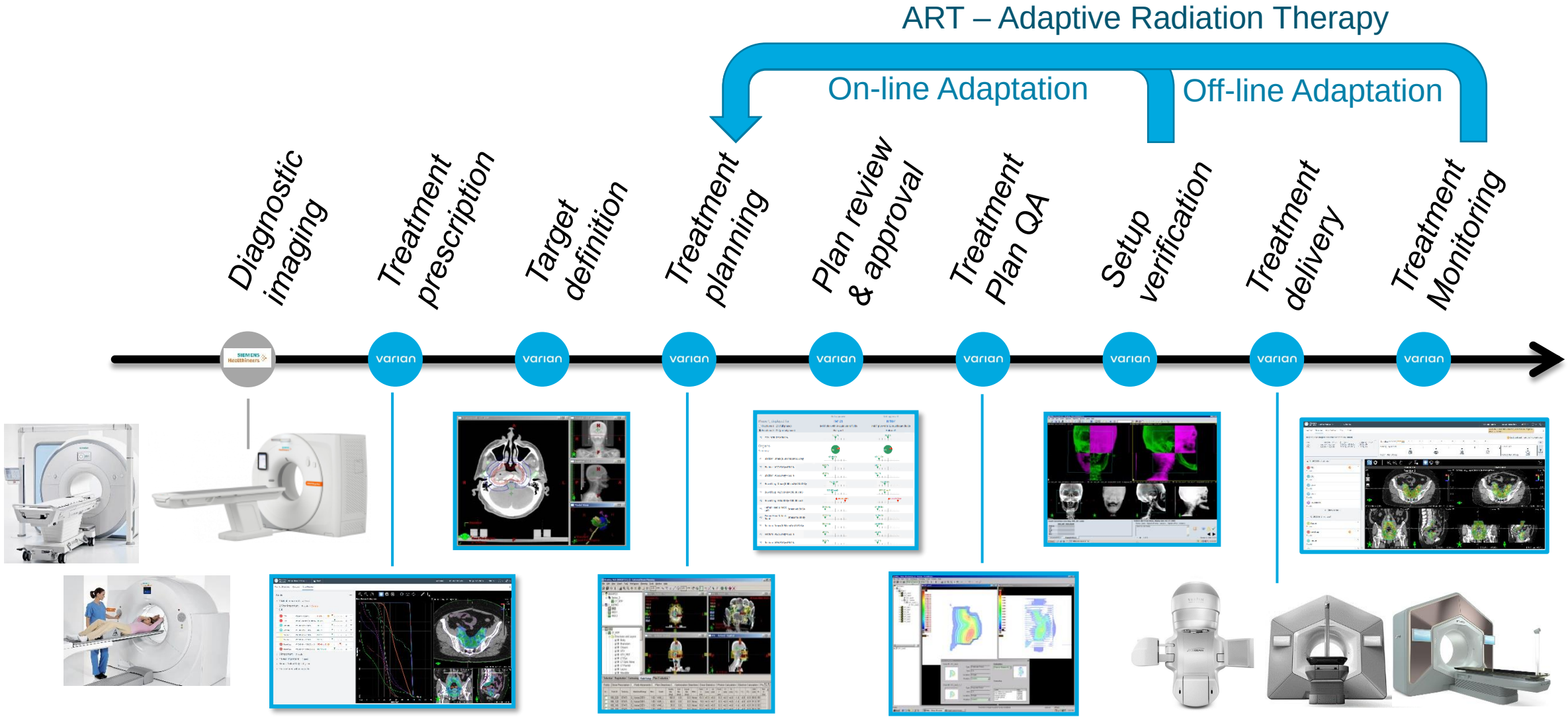
Typical Radiation Therapy Process



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High Energy X-Ray's

Energies used in Radiation Therapy

Co-60: 1.25 MeV

TrueBeam (choose from 9 X-ray, 8 electron energies):

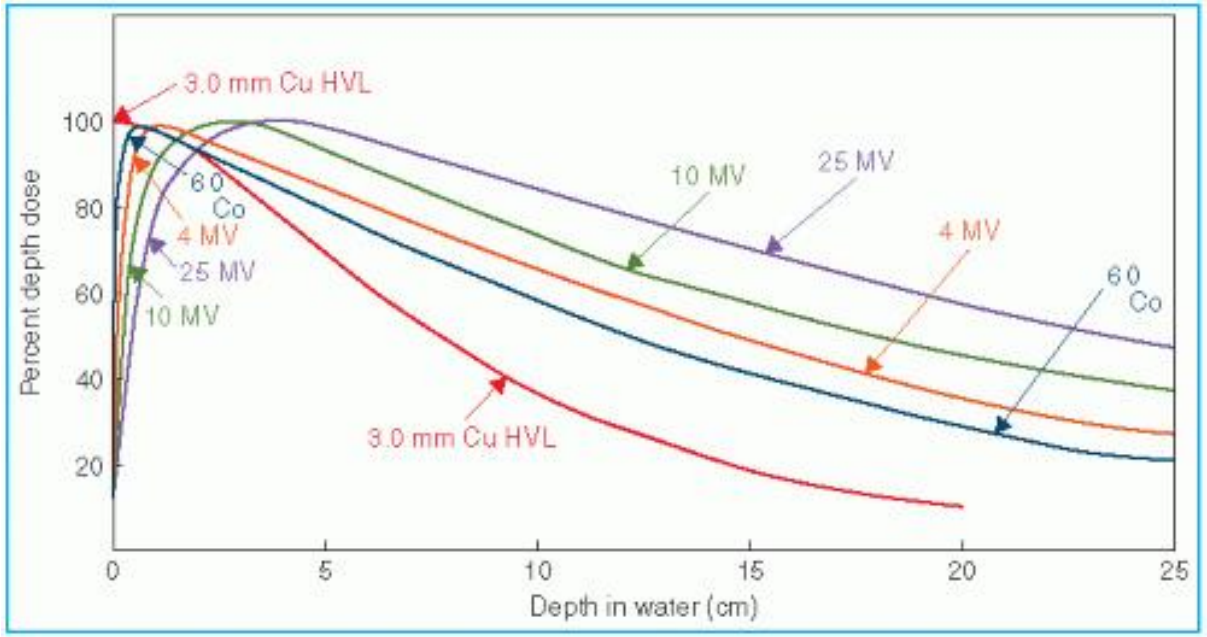
- 4 – 25 MV, 400 – 2400 MU/min*
- 6 - 22 MeV Electrons, 1000 – 2500 MU/min

Halcyon:

- 6 MV, 800 MU/min
- No Electrons

ProBeam:

- 70 – 245 MeV Protons, >2Gy/liter/min



TrueBeam

Halcyon

* MU: 100 MU delivers 1 Gy under reference conditions (10x10 cm^2 field size, 100 cm source distance)

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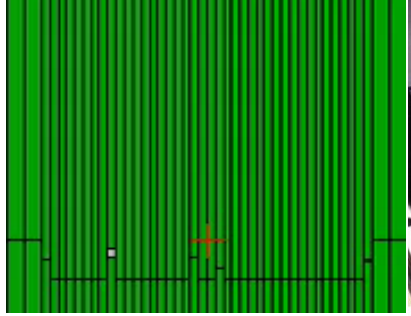
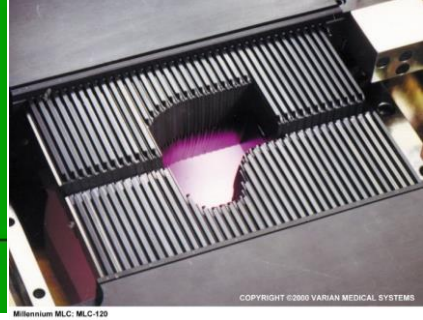
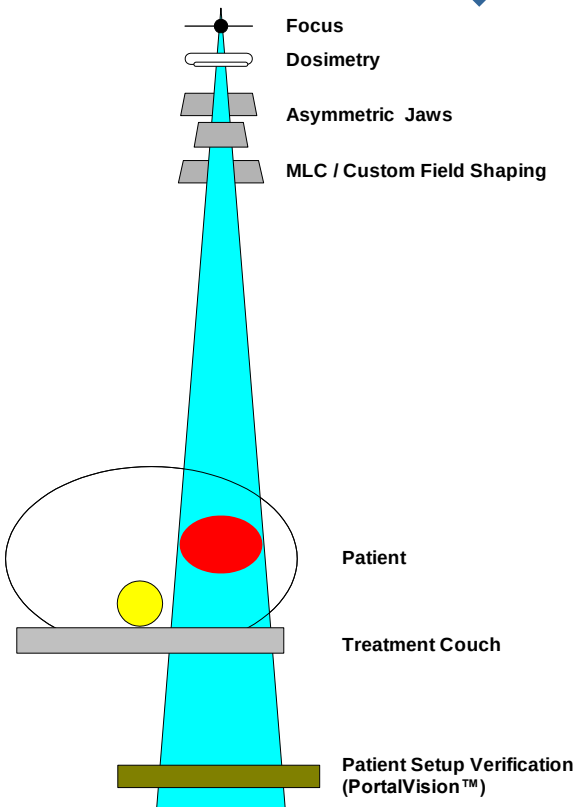
Dose Concentration within the Patient

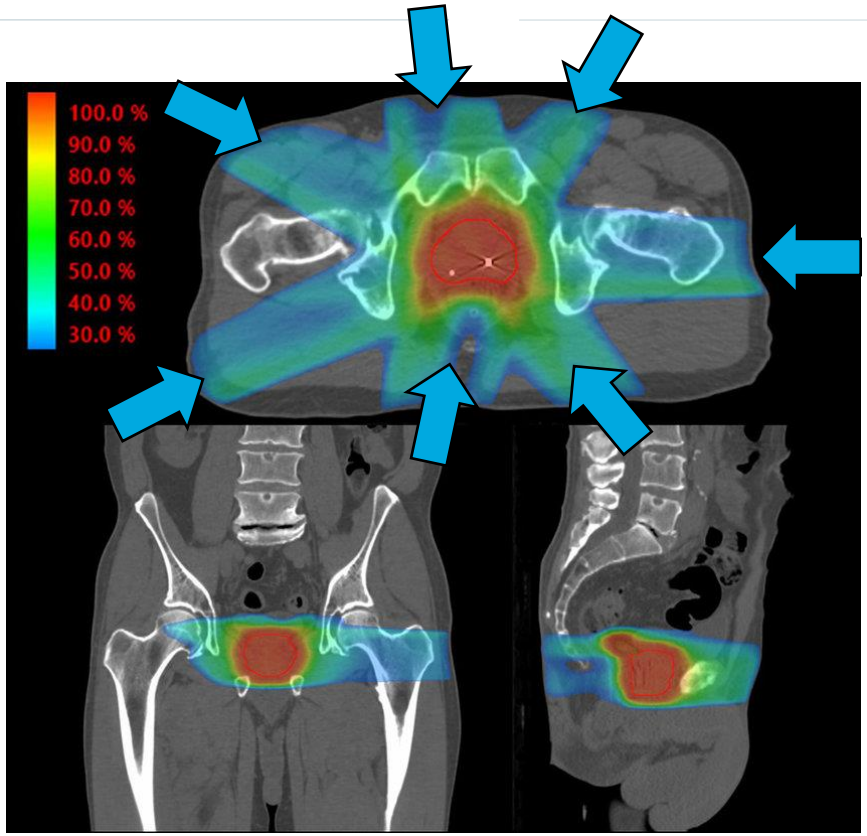
How to accumulate the dose in the tumor?





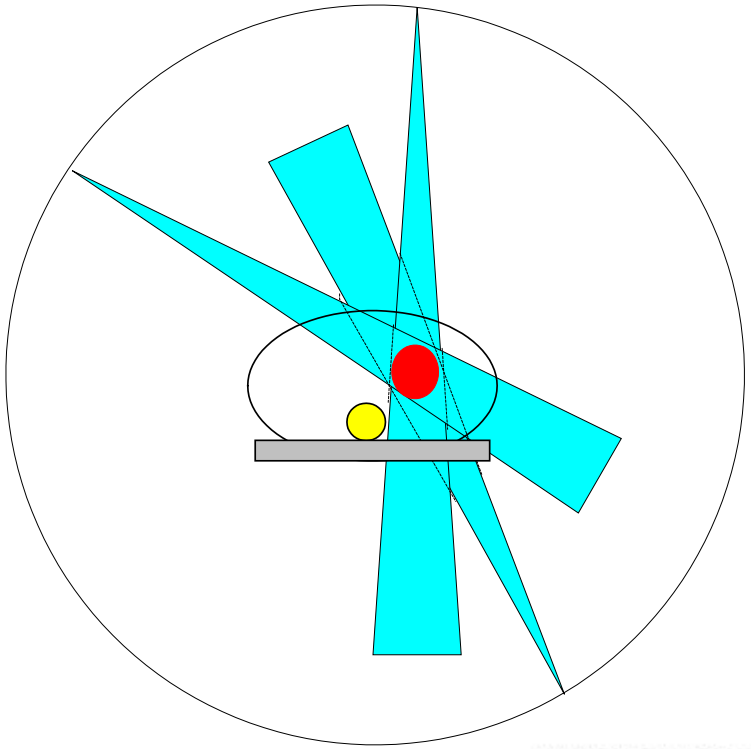
Static Field





7 Field IMRT Prostate Treatment

Multiple Fields



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Innovation Milestones

With a focus on linear accelerators

The Future begins here

Ethos Adaptive Therapy

Halcyon 6 MV

Calypso Real Time Tracking System

EDGE Radiosurgery™

TrueBeam™ - Radically Different

RapidArc®, Enhanced SBRT & Neurosurgical Apps

IGRT, Systems Integration, DART

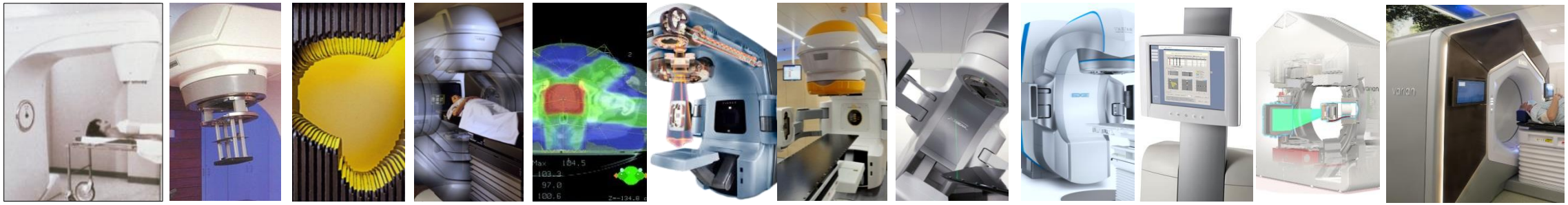
IMRT, Integration & Process Enhancements

Dynamic Conformal Techniques

Computerization of Linacs, MLCs & 3D Planning

Exploration of High Energies & Electrons

Basic Medical Accelerator Designs Developed & Proved



1960s 1970s 1980s 1990s 1995 2000s 2007 2010 2013 2013 2017 2020 ?

Quality of accelerator, power generators, RF and vacuum components is key to guarantee reliability and uptime in clinical service. Some linacs are more than 15 years in the field.

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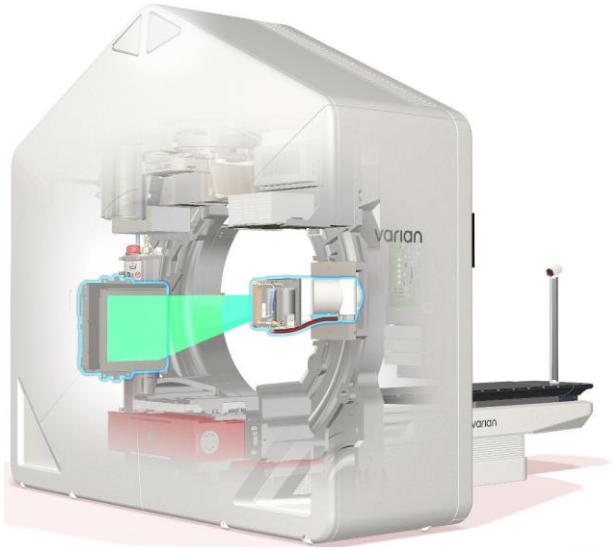
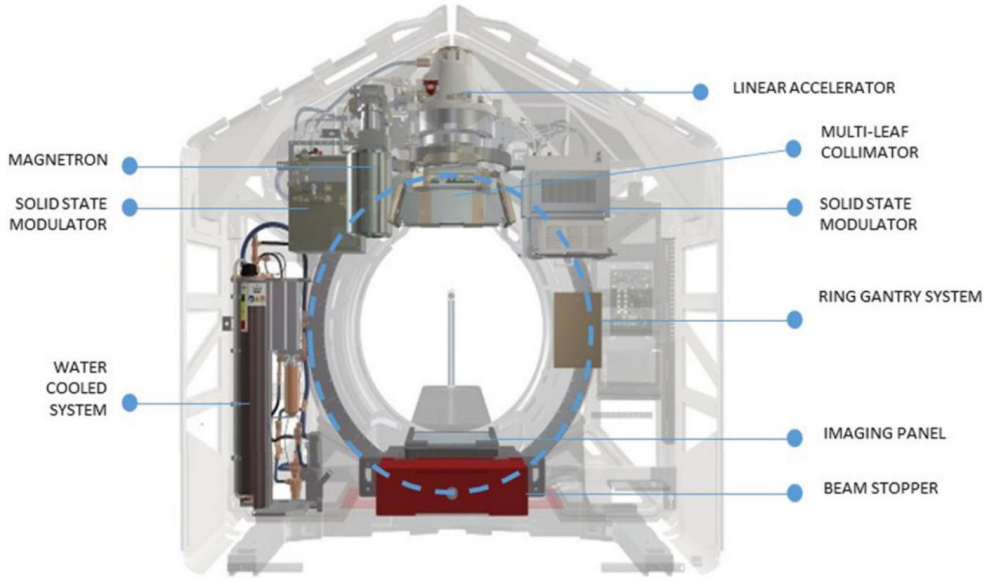
2017 Halcyon and 2020 Ethos Introduction

Varian's newest cancer treatment device and adaptive RT platform

- Image-guided volumetric intensity-modulated radiotherapy (IMRT, VMAT)
- Up to 4x faster gantry rotation
- Image and treat in just 9 steps
- Install in 14 days or less
- Commissioned treatment planning system
- Improve clinical efficiency
- Streamlined adaptive RT Workflow
- Fast Innovation Cycles





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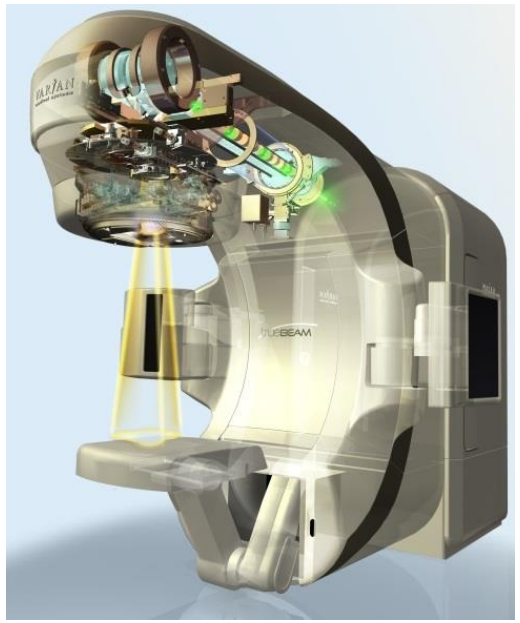
High Energy X-Ray Clinical Treatment Delivery Devices

In clinical operation worldwide today (approximate numbers)

Total Number of clinical high energy X-ray treatment delivery devices in clinical operation: ~15’000
Varian and Siemens have a market share of over 60%

Clinac

TrueBeam



Halcyon / Ethos

Siemens

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Varian Vision in light of the worldwide Cancer Burden

And how to realize it

Quality

Complaint and Post Market Safety KPIs

Predictability

Project and Program Execution KPIs

Accelerate Innovation

Applied Research Initiatives / Technology Innovation Model / FDA Submission Cadence

Product Improvement

Delivery Systems Machine Faults by Version

Simplicity

DevOps Continuous Integration/Continuous Development KPIs

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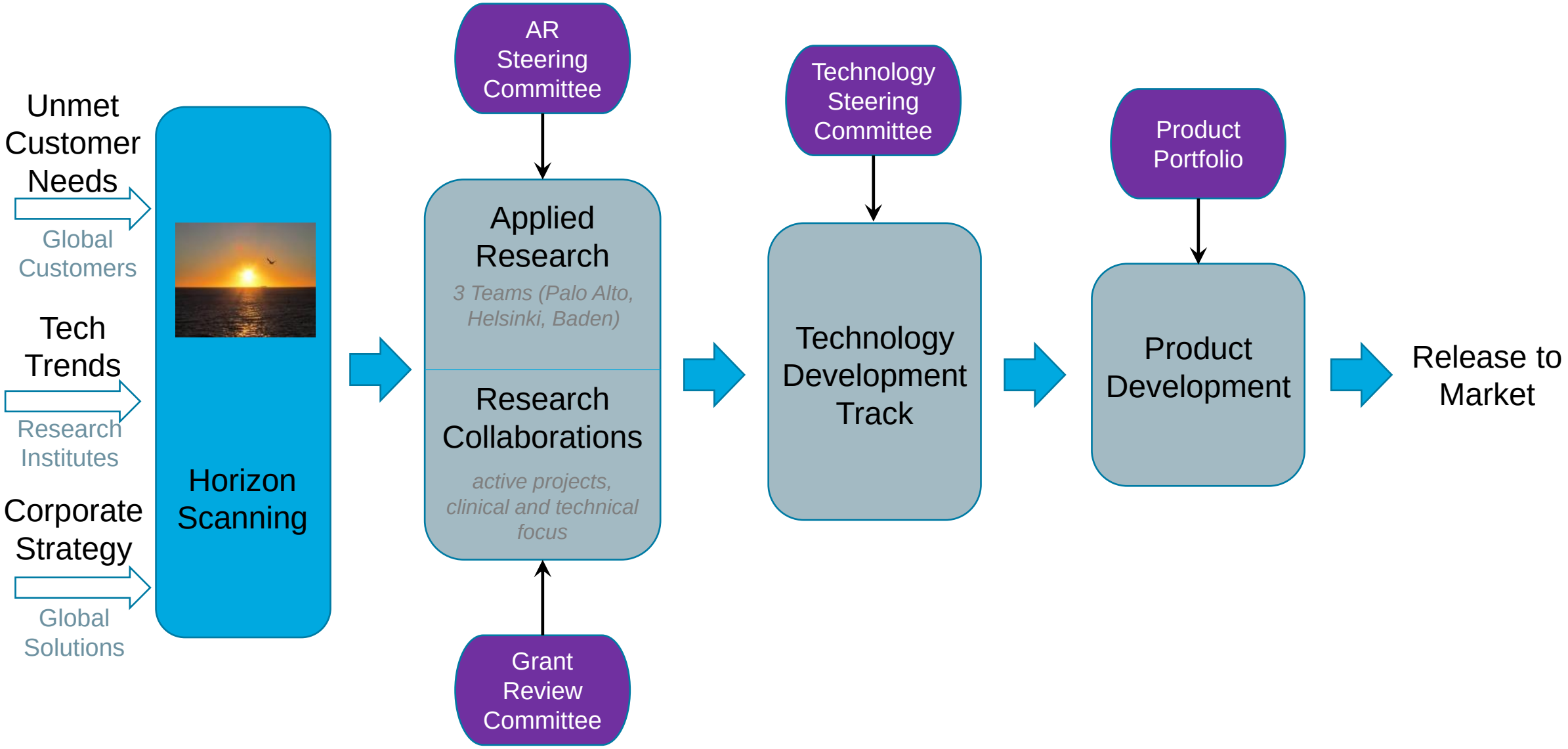
Varian R&D Innovation Process - Overview



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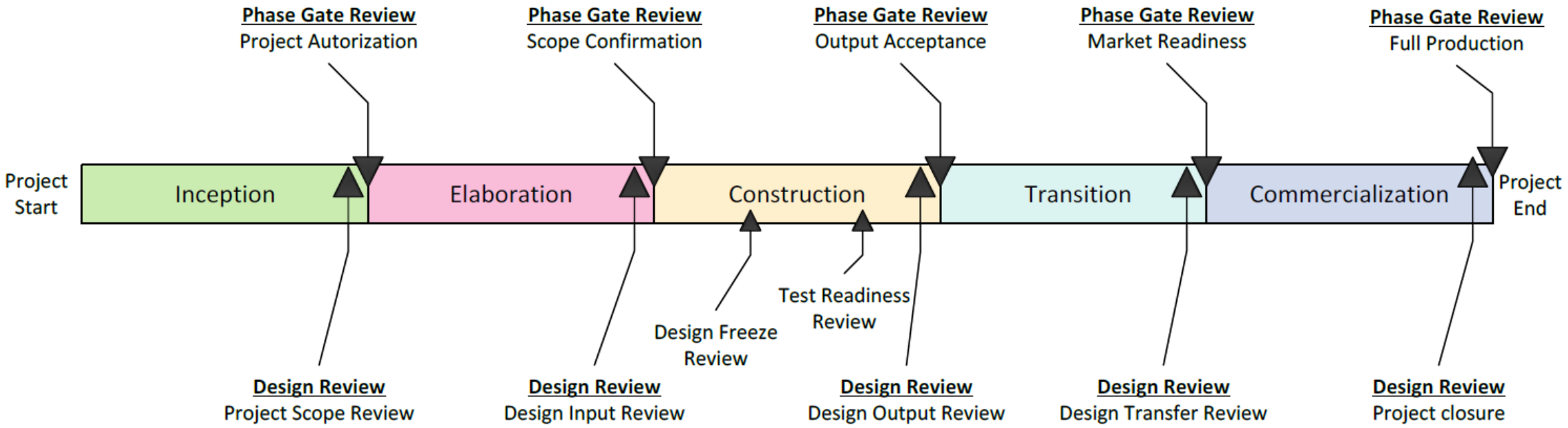
Design and Development Procedures

A lot of documents and meetings

- Ensure device design and development is planned, controlled, managed, and documented from initial definition through completion, manufacturing and service
- Include post-market changes, maintenance, and obsolescence
- Continuous engineering after market release
- Obsolescence engineering



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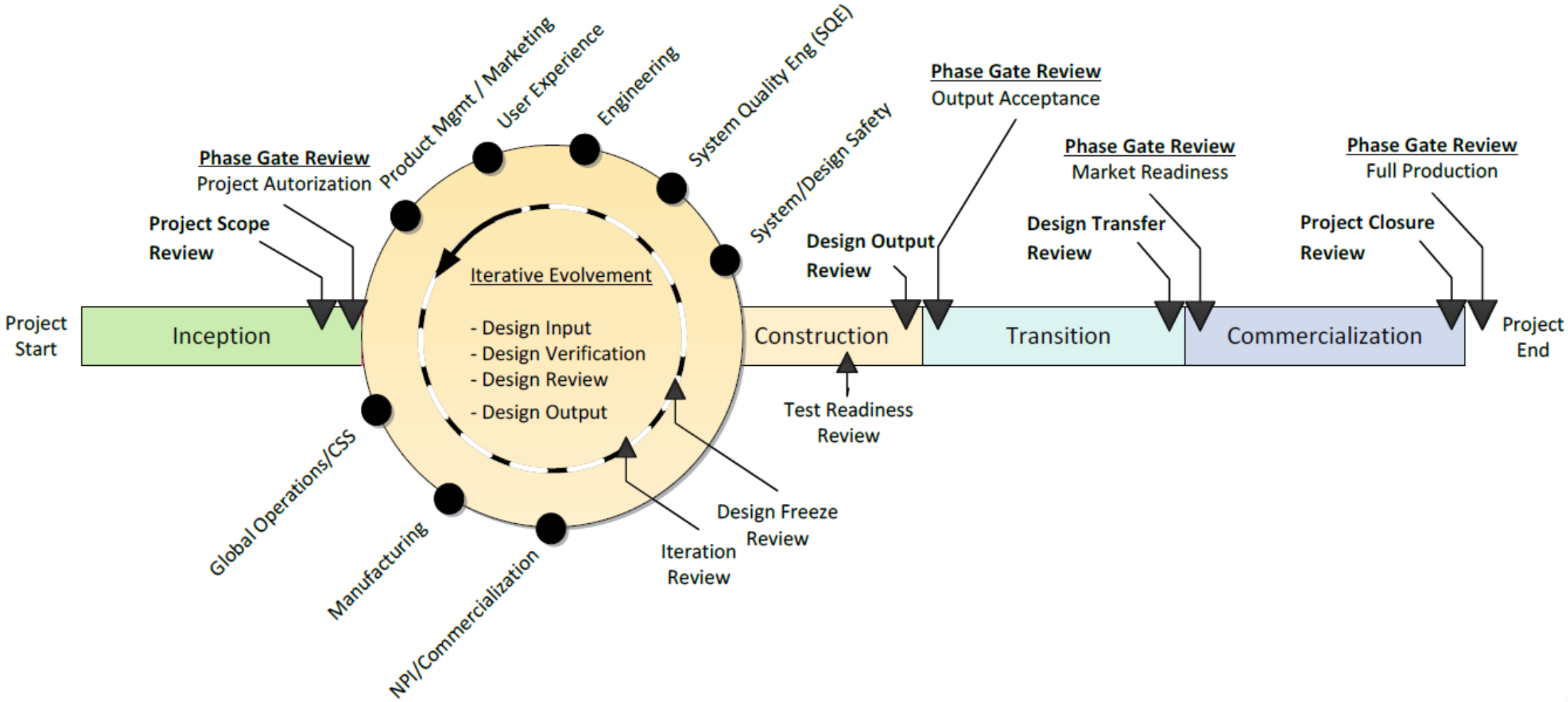
Iterative Design and Development Methodology

An agile and “non-linear” approach



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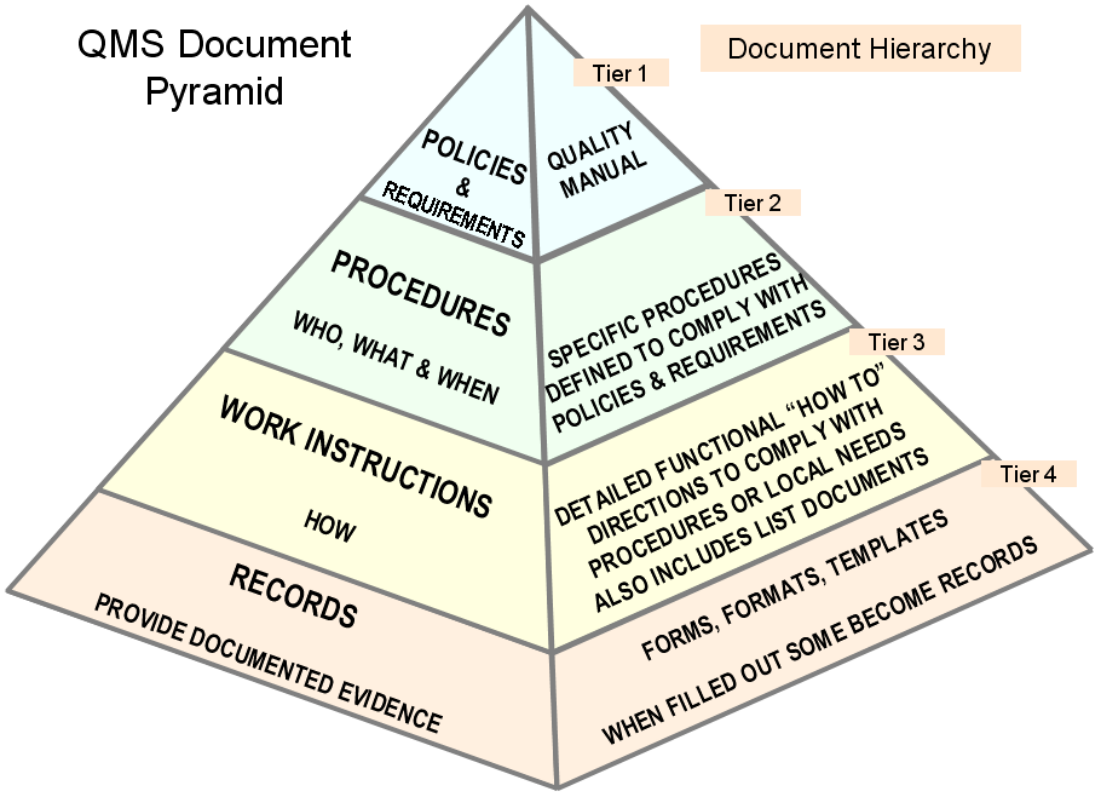
Quality Management System

- Ensure compliance with
  - EN ISO 13485: 2003 (new: 2016) Medical devices, Quality Management Systems, Requirements for Regulatory Purposes
  - US Food and Drug Administration, Quality System Regulation, 21 CFR Part 820
  - EU Medical Device Directive 93/42/EEC
  - Other important quality system supporting standards and regulations:
    - IEC 60601-x (Harmonized Standards[1])
    - FDA device regulations[2]
      - 21 CFR 803 Medical Device Reporting
      - 21 CFR 806 Correction & Removal
      - 21 CFR 807 Establishment Registration and Device Listing for Manufacturers and Initial Importers of Devices
      - 21 CFR 11 Electronic Records and Electronic Signatures
    - Country specific quality system regulations



[1] http://ec.europa.eu/growth/single-market/european-standards/harmonised-standards/medical-devices/

[2] https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/overview/default.htm

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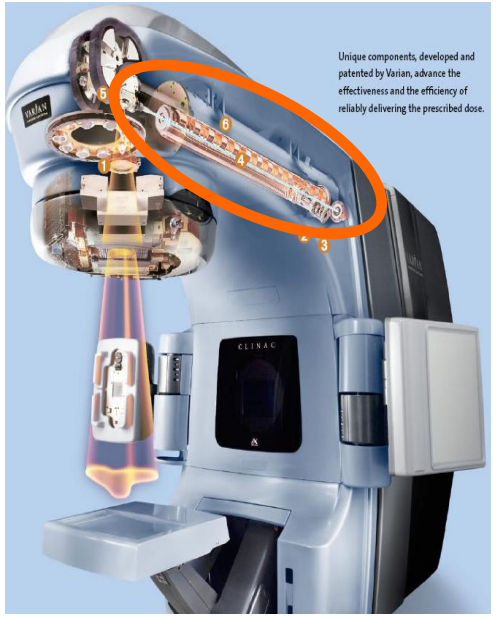
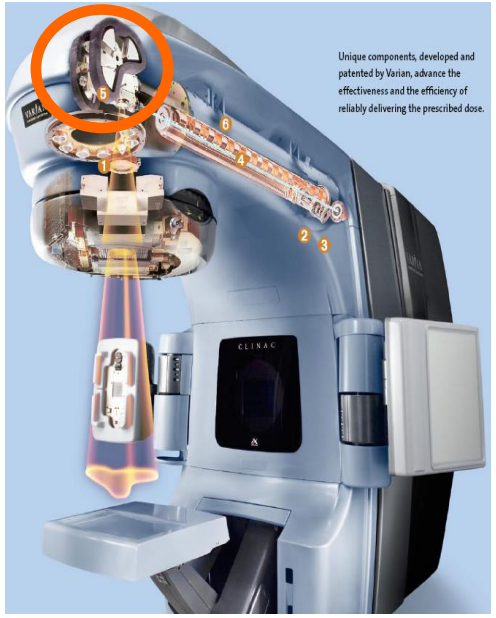
Linear Accelerator Development and Components

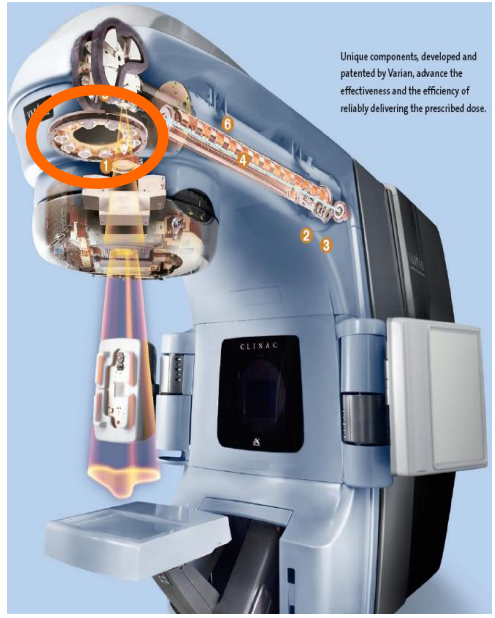
Accelerators used to be much too big



Linear electron accelerator or guide

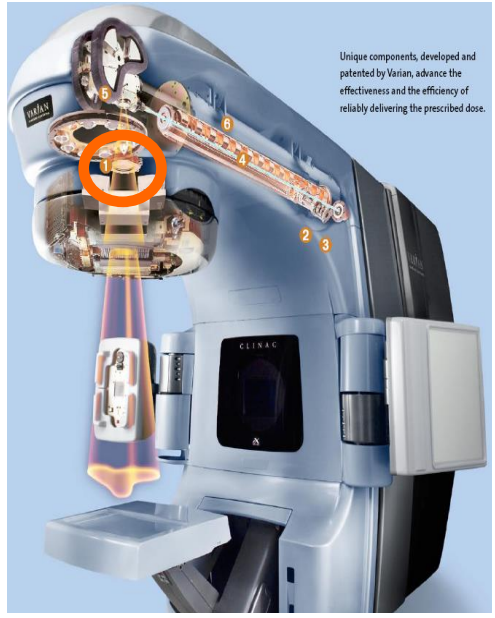


Beam Transport: The Bend Magnet



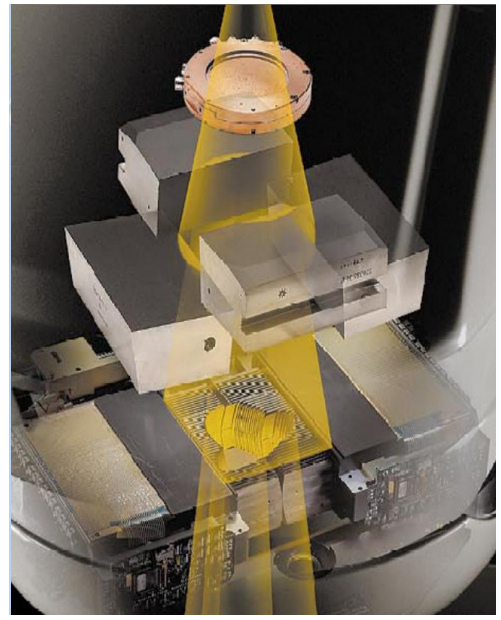
e-Scattering Foils and X-Ray Flattening Filters

- Scatter e-beams and flatten X-Ray beams to make the field uniform at the patient



Ion Chamber

- Monitor dose delivered to the patient



Collimate and shape the X-ray Beam

- Limit the extent of the beam – only treat the tumor

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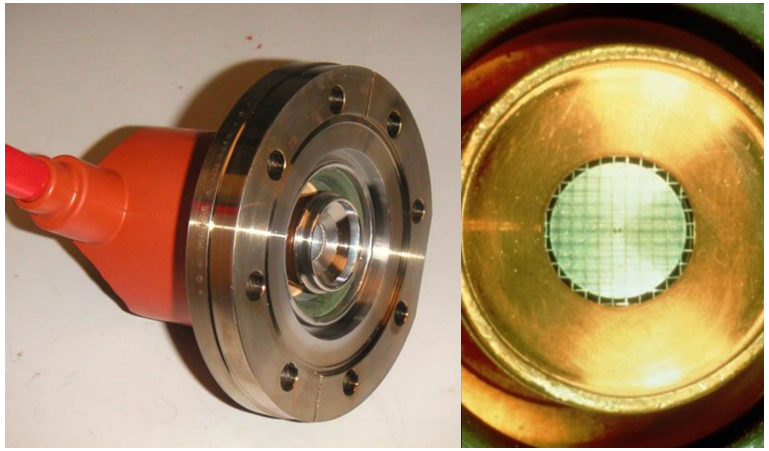
High Energy Electron Linear Accelerator

From high energy electrons to X-ray's

Gridded Triode Electron Gun

5-25 kV DC, up to 1 amp

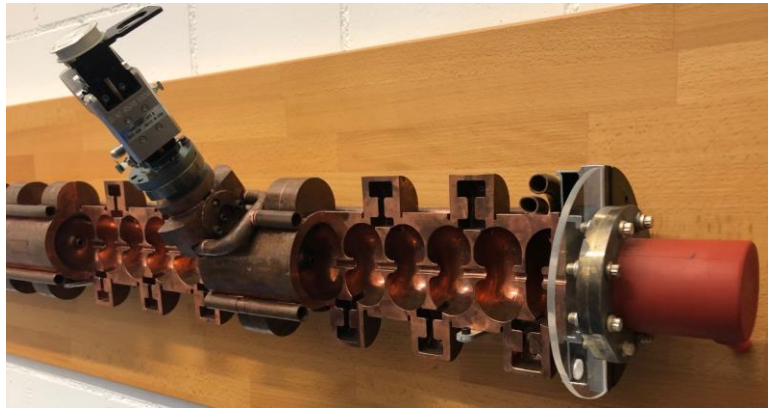
~500 k Electrons per bunch

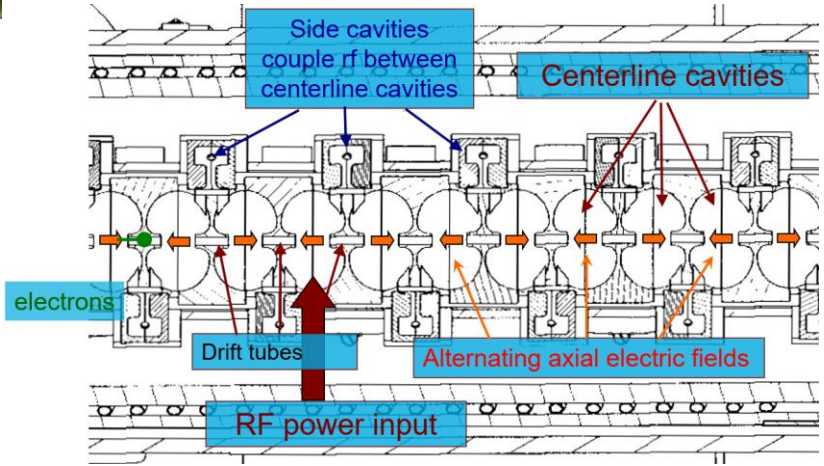


- No dark current (using the grid)
- Filament & cathode remain hot for stable operation

Linear Accelerator Structure

Side coupled standing wave accelerator





High Power RF Klystron ~3 GHz, 5.5 MW peak (high energy), 5 kW average (dose rate)

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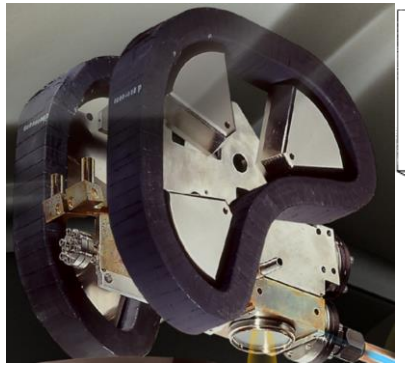
High Energy Electron Linear Accelerator

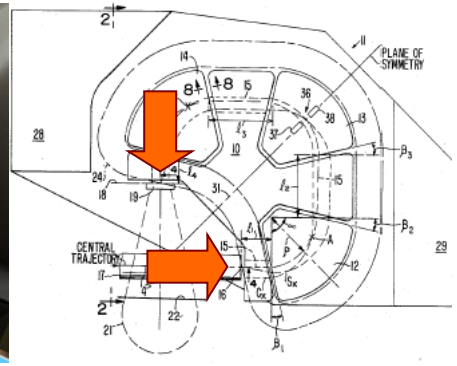
From high energy electron to X-ray production

Bending Magnet (~17 kGauss)

achromatic & non-dispersive beam steering/focusing is independent of energy

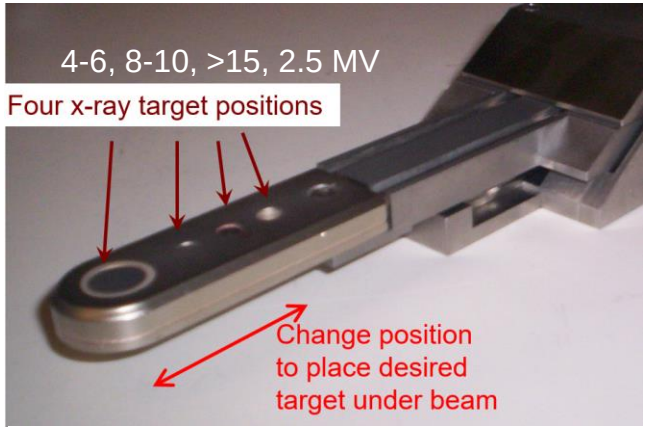
1-to-1 imaging (radial, transverse) of beam

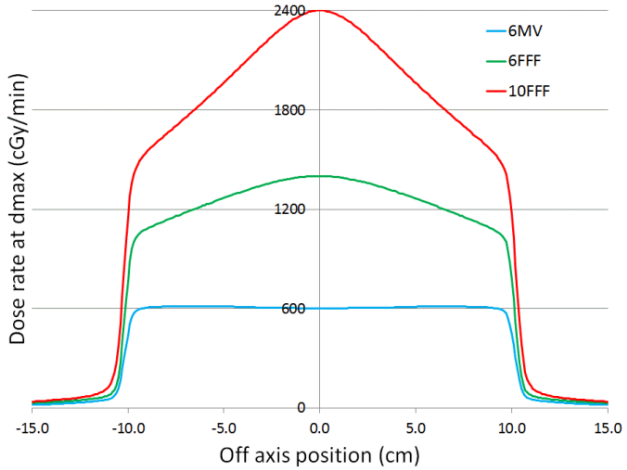




- 270-degree, 3-sector (pole), uniform pole gap, achromatic, bending magnet
- ± 3% energy slits
- Long-term energy stability
- Direction and position independence (easy to adjust)
- Small, circular x-ray spot
  - Sharp penumbra
  - Good imaging

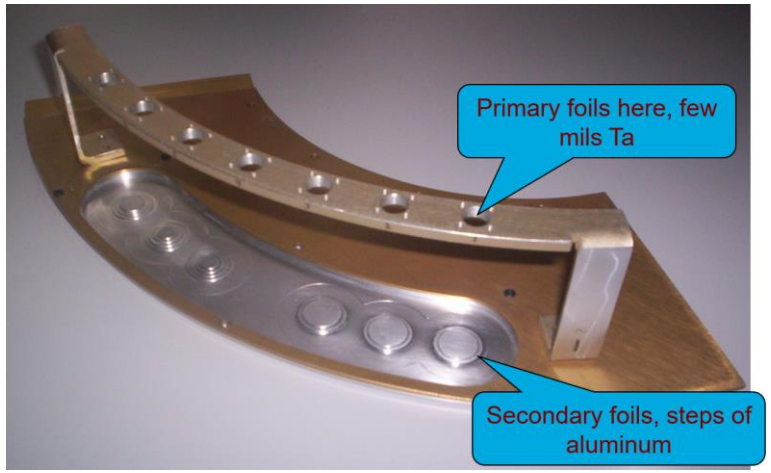
X-Ray Transmission Target Retracted for Electron Mode

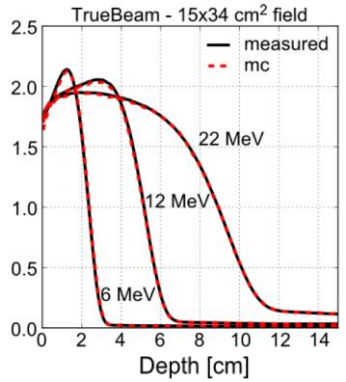




Electron Double Scatter System for Electron Mode

Requires ~ 1 mil positioning accuracy





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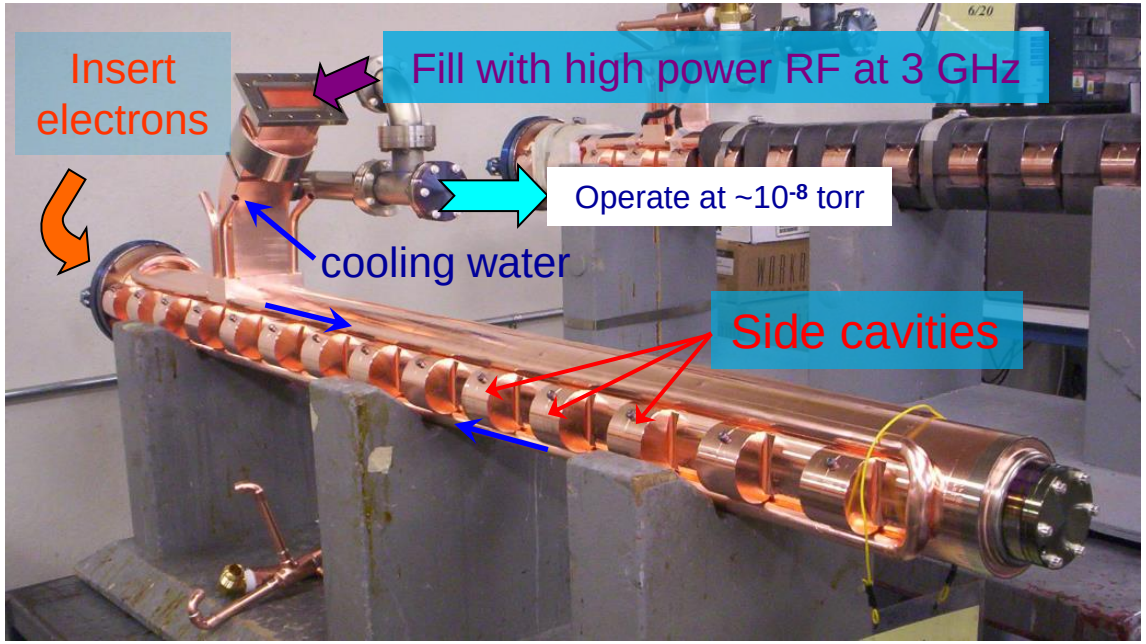
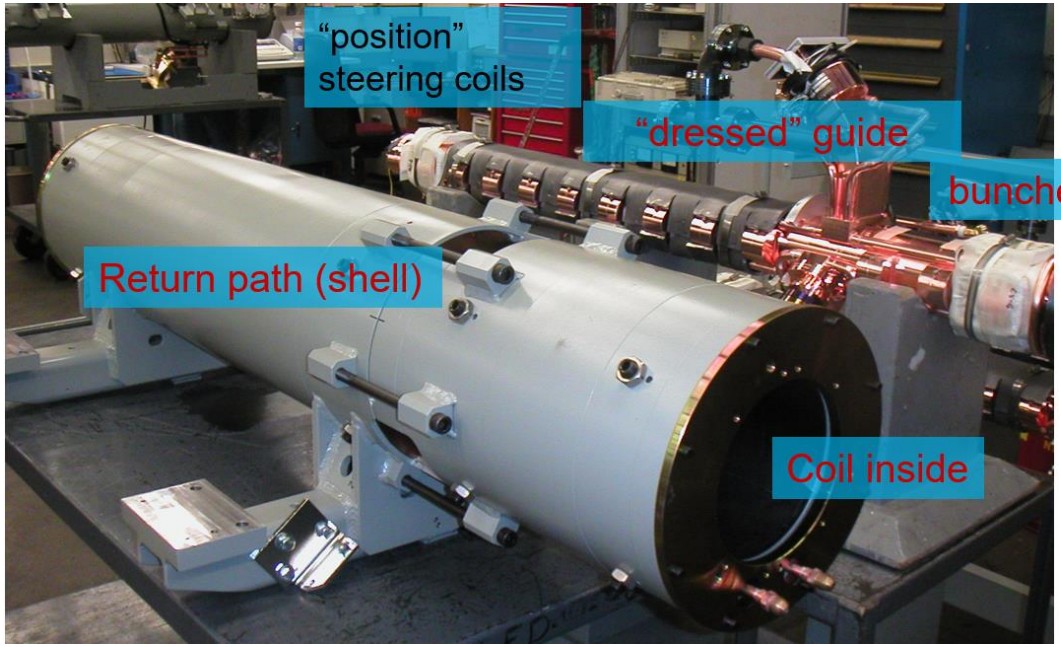
Side-coupled standing-wave Electron Linear Accelerator

~1.5 m, 28 ½ cavities



Solenoid: 5 kW, <~ 1kGauss on axis

Compensate for magnetic, structural anomalies



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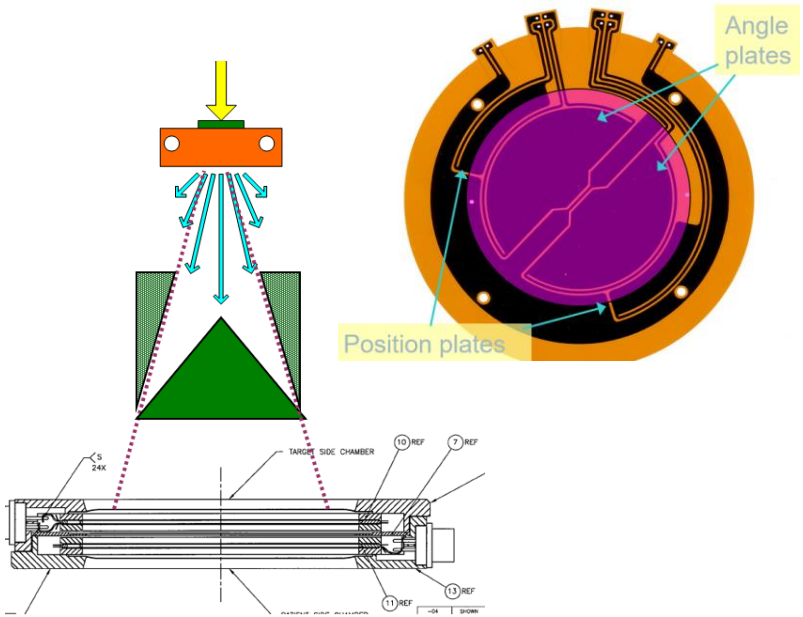
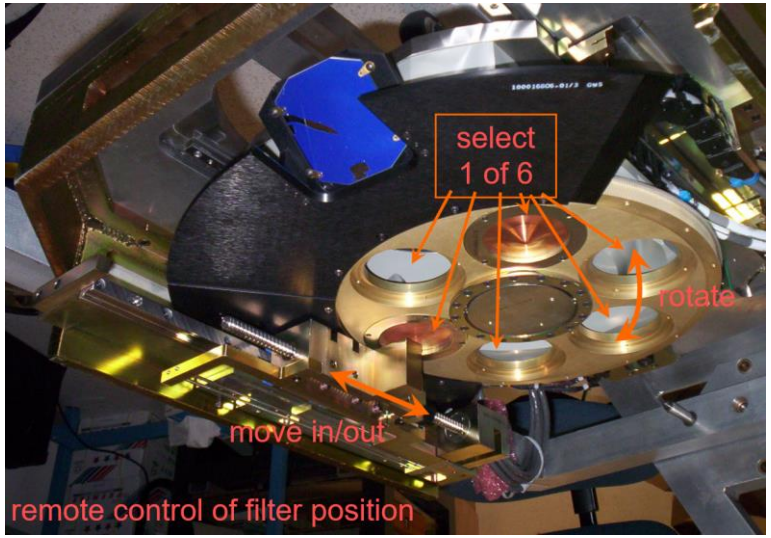
Head of the Electron Linear Accelerator

Transmission Ion Chamber
for dose and beam position monitoring

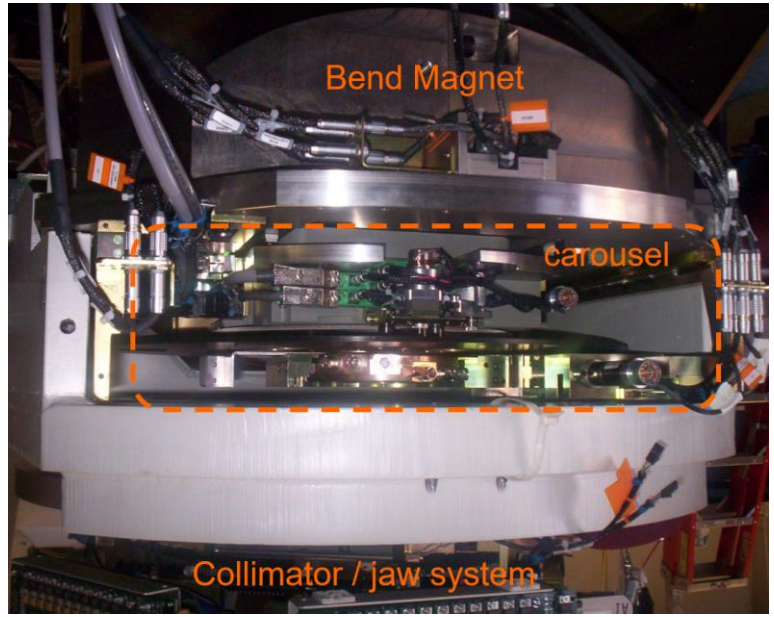


Filter Carousel
Choose correct flattening filter or electron mode



Carousel rotates and translates to position required elements in beam line

Front View of Head



varian
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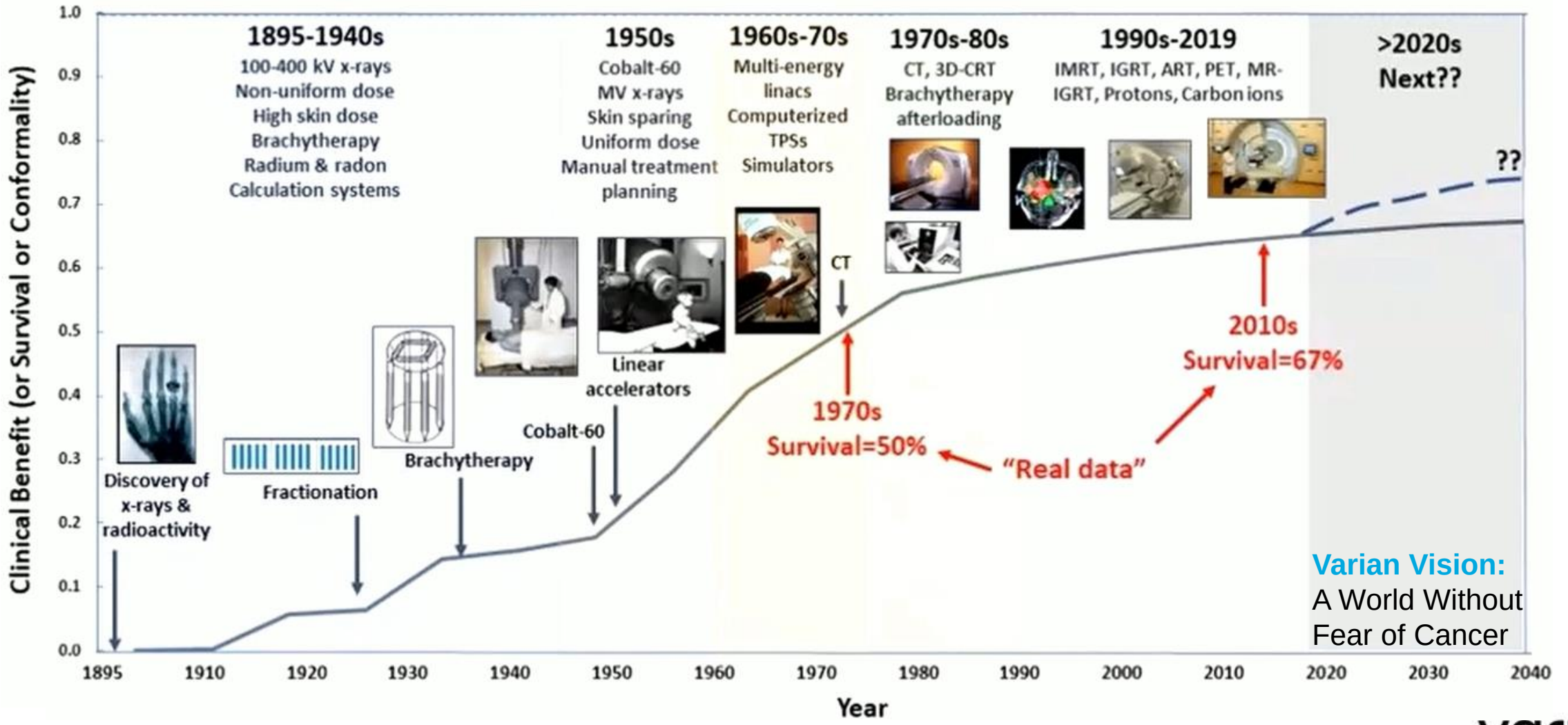
Van Dyk – The Modern Technology of Radiation Oncology, Volume 4

Varian and Siemens Healthineers are planning to impact the future …



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(Thank you)

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