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Careflow with an integrated future

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Accelerators for Hadrontherapy and the Role of Industry

Particle Therapy
Siemens AG
Healthcare Sector

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Overview

- Particle Therapy – Evolution and Market
- Particle Therapy - Applications
- Know How Transfer - from Research to Healthcare
- Market Players & Collaborations
- Future Research Topics

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Evolution and Market

History of Radiation Therapy with Ions

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Today: **Particle therapy is applied in purely clinical centers, e.g.**

- Francis H. Burr PTC, Boston; MD Anderson, Houston; University of Florida; U. Penn.
- HIT, Heidelberg; Rhön Klinikum AG, Marburg; CNAO, Milano; RPTC, Munich; Essen ; Kiel
- HIBMC, Hyogo; NCC, Kashiwa; Shizuoka; PMRC, Tsukuba

1996/97 **First tumor conform radiation with scanned beam – protons at PSI (Villigen, Switzerland), ^{12}C-Ions at GSI (Darmstadt, Germany)**

1993 **First center for ^{12}C-ions therapy in Chiba (Japan)**

1990 **First center for proton therapy in Loma Linda (USA)**

1975 **LBL irradiated for the first time with ions (helium, carbon, neon)**

1974 **First proton therapy at the Harvard Cyclotron**

1957 **Uppsala started with proton treatment**

1954 **LBL (Lawrence Berkeley Laboratory, USA) started radiotherapy for deep located tumors with protons**

1946 **R. R. Wilson proposed charged particles (p, ions) for applications in radiotherapy**

Evolution and Market
What are the Treatment Options?

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Localized Tumors: 58%

Metastazised Tumors: 42%

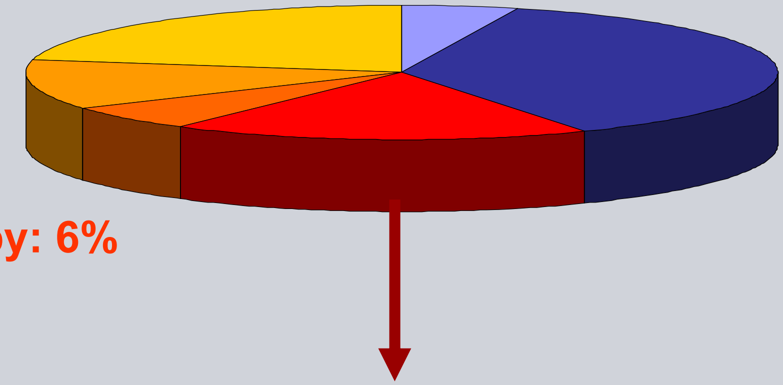
Surgery: 22%

Chemo Therapy: 5%

Conventional Radiotherapy: 12%

Palliative Therapy: 37%

Surgery & Radiotherapy: 6%



Failure of Local Therapy 18%

Evolution and Market

Estimation of Patient Numbers and PT Centers

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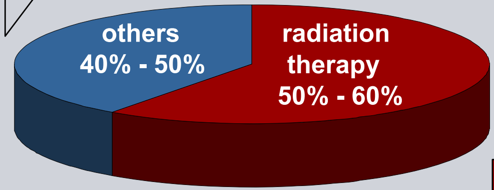
Germany:
New cancer patients p.a.

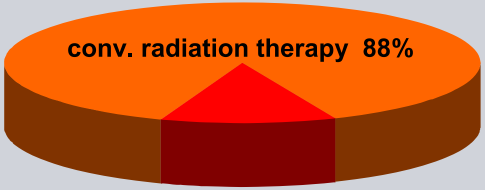
425,000 new patients

Share of radiation therapy from all cancer treatments



212,500 patients

Share of particle therapy from radiation therapy



particle therapy 12%
(5% to 20% according to other investigations)

25,500 patients

Number of PT centers

10 centers based on 2500 patients p.a.

Europe: 1.7 Mio. patients | **850,000 patients** | **102,000 patients** | **40 centers**

⇨ About 1 particle therapy center per 10 million inhabitants

References: Epidemiology: Robert-Koch-Institut, 2006; radiotherapy: National Cancer Institute, US National Institutes of Health; particle therapy: MedAustron, Etoile

Siemens Particle Therapy products and solutions are works-in-progress and require country specific regulatory approval prior to clinical use.

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Applications

Reported Common Properties of Protons and Carbon Ions

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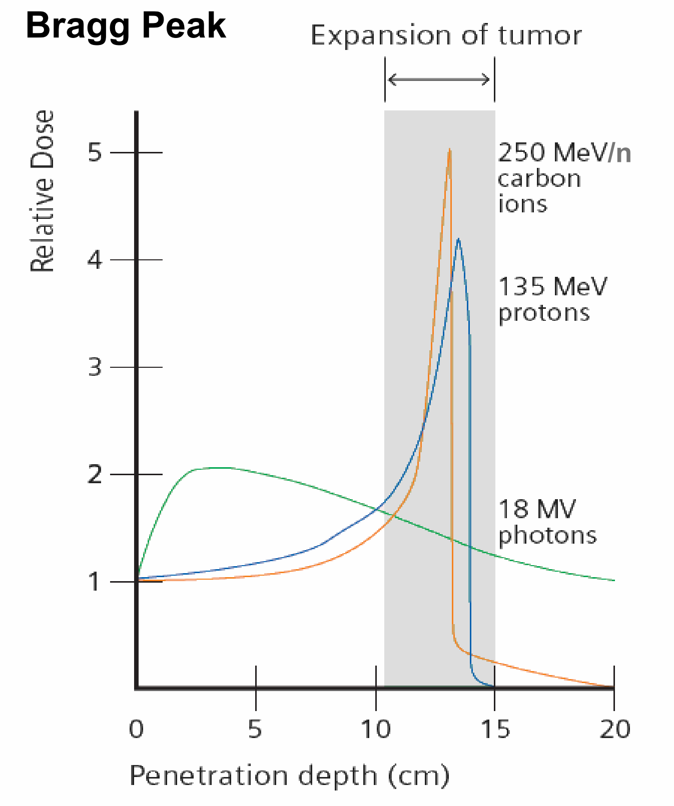
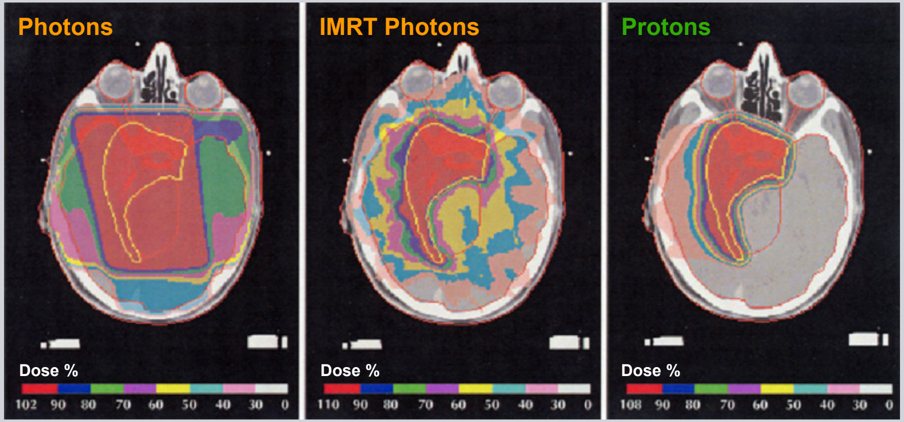


Objectives:

- **Increase of conformity and reduction of integral dose (less interactions with normal tissue, higher quality of life after successful treatment)**
- **Improve local control rate (less recurrent tumors)**
- **Higher survival rate**



Courtesy of A. Lomax, Paul Scherer Institur, Villigen, Switzerland, - Data on file

Applications
Reported Clinical Consequences of Protons and Carbon Ions

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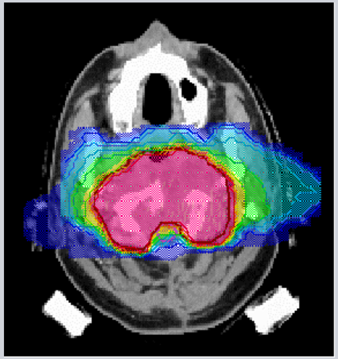
Higher target conformity due to physics properties of p and ^{12}C (active scanning as precondition)

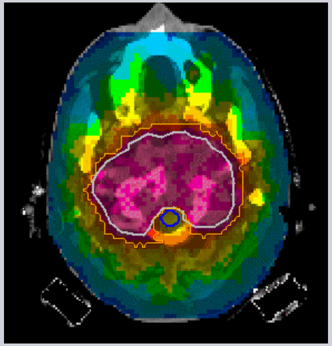
- High dose in tumor volume due to inverse dose profile
- Less scattering for ^{12}C
- Reduced dose in organs at risk and healthy tissue



Carbon ions (2 beams)

New applications thanks to the biological characteristics of ^{12}C

- Radiation resistant tumors
- Slow growing tumors
- Hypoxic tumors



IMRT (9 beams)

Clinical results

- Low toxicity – low integral dose (p and ^{12}C)
- Higher tumor control rates, especially for the aforesaid tumors (^{12}C)
- Reduction of fractionation scheme possible (^{12}C)

Courtesy of the University Hospital, Heidelberg and GSI, Darmstadt

Courtesy of GSI

Applications

How does the Clinical Application Impact the Technical Realization?

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Requirements of a medical operator	Technical Realization
Best target conformity	▪ Scanning ▪ Active energy selection ▪ Avoid scattering
Short treatment times	▪ High intensity in accelerator, short accelerator cycle times
High beam availability	▪ Fast switching between rooms and ion species ▪ No field-specific beam modifiers ▪ High system (accelerator) uptime
Techniques to treat moving organs	▪ Gating ▪ Tracking (research) ▪ Multi painting (research)

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Know How Transfer – from Research to Healthcare

Examples of Research Collaborations

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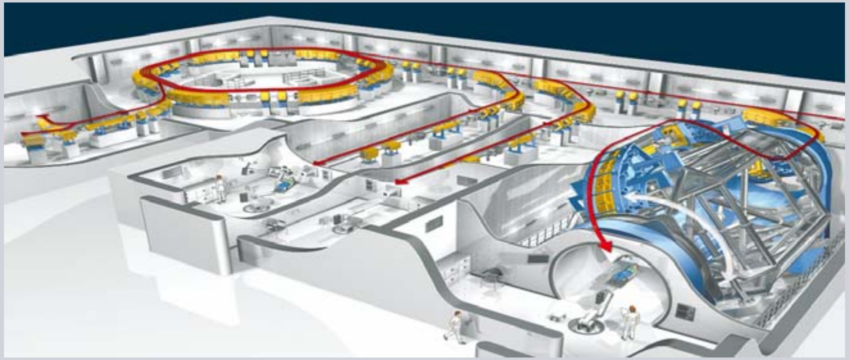
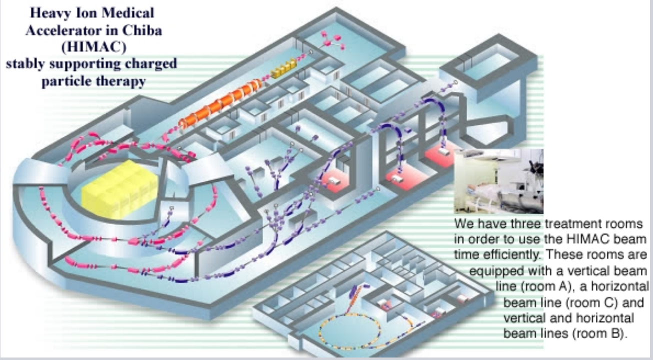


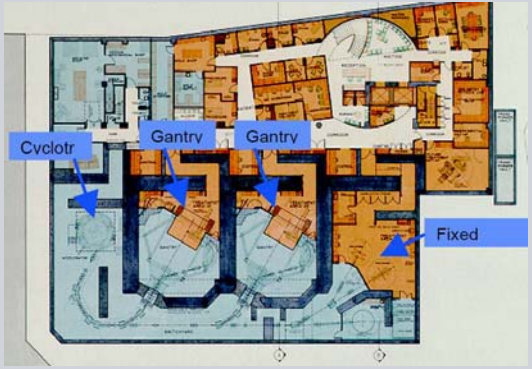
University of Heidelberg, Germany / GSI and Siemens



NIRS Chiba, Japan / Mitsubishi, Hitachi, Sumitomo

MD Anderson Houston, USA / Hitachi

PSI Villigen, Switzerland / Varian-Accel



MGH Boston, USA / IBA

Know How Transfer – from Research to Healthcare

Example: Accelerator Design from GSI to Siemens AG/Danfysik

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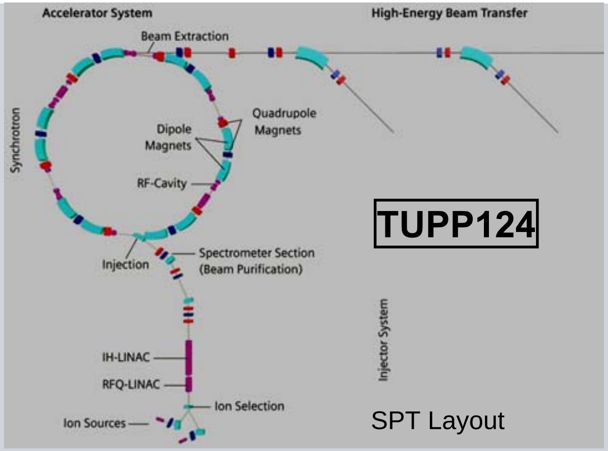


SPT Layout

The HICAT (GSI) accelerator design has been revised

- to reduce construction and operating costs
- to improve technical capabilities
- cooperation of Danfysik / GSI / Siemens

Design changes in the Synchrotron layout

- Fully symmetric lattice
- Lattice type changed from Doublet to FODO → reduction of quadrupole gradient by 30%, smaller β functions, smoother lattice, reduced dipersion function, larger acceptance
- 12 dipoles (each 8 tons) instead of 6 (each 25 tons) → easier installation and handling
- Smaller and lighter quadrupoles
- Optimized injection and extraction system
- Improved in terms of power consumption

Know How Transfer – from Research/Industry to Healthcare

Example: Accelerator Design from GSI to Siemens AG/Danfysik

Standardization of components

- E.g. Standardization of dipoles and quadrupoles, power supplies

  → reduction in construction costs, advantages in terms of serviceability.

Service and maintenance concept

- IT Support (Service Software, Service workflow,…)
- Optimized spare part storage
- Condition based maintenance concept (trending, collection of process data) → high uptime

Courtesy of the University Hospital of Heidelberg, Germany

From Research/Industry to Healthcare

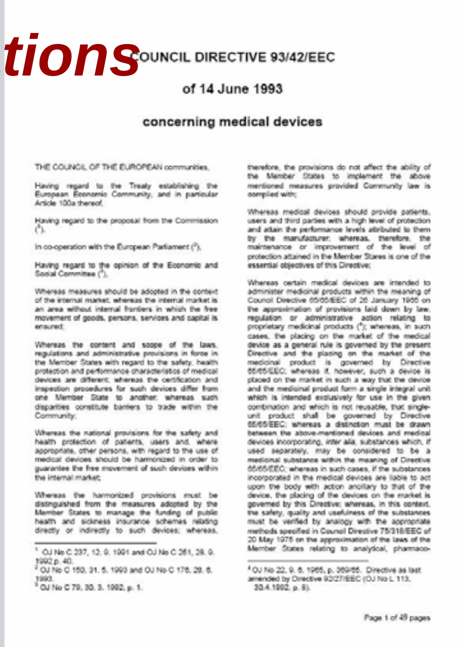
What distinguishes a Medical Device from an Industrial Product?

Apply highest Standards for safety and the security for the patient

Establish a safety concept for the entire system including the accelerator system.

Implement adequate interlock and spill-abort systems.

Follow applicable medical standards, rules and regulations



COUNCIL DIRECTIVE 93/42/EEC

of 14 June 1993

concerning medical devices

THE COUNCIL OF THE EUROPEAN communities,

Having regard to the Treaty establishing the European Economic Community, and in particular Article 100a thereof,

Having regard to the proposal from the Commission (1),

In co-operation with the European Parliament (2),

Having regard to the opinion of the Economic and Social Committee (3),

Whereas measures should be adopted in the context of the internal market; whereas the internal market is an area without internal frontiers in which the free movement of goods, persons, services and capital is ensured;

Whereas the content and scope of the laws, regulations and administrative provisions in force in the Member States with regard to the safety, health protection and performance characteristics of medical devices are different; whereas the certification and inspection procedures for such devices differ from one Member State to another; whereas such disparities constitute barriers to trade within the Community;

Whereas the national provisions for the safety and health protection of patients, users and, where appropriate, other persons, with regard to the use of medical devices should be harmonized in order to guarantee the free movement of such devices within the internal market;

Whereas the harmonized provisions must be distinguished from the measures adopted by the Member States to manage the funding of public health and sickness insurance schemes relating directly or indirectly to such devices; whereas, therefore, the provisions do not affect the ability of the Member States to implement the above mentioned measures provided Community law is complied with;

Whereas medical devices should provide patients, users and third parties with a high level of protection and attain the performance levels attributed to them by the manufacturer; whereas, therefore, the maintenance or improvement of the level of protection attained in the Member States is one of the essential objectives of this Directive;

Whereas certain medical devices are intended to administer medicinal products within the meaning of Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (4); whereas, in such cases, the placing on the market of the medical device as a general rule is governed by the present Directive and the placing on the market of the medicinal product is governed by Directive 65/65/EEC; whereas if, however, such a device is placed on the market in such a way that the device and the medicinal product form a single integral unit which is intended exclusively for use in the given combination and which is not reusable, that single-unit product shall be governed by Directive 65/65/EEC; whereas a distinction must be drawn between the above-mentioned devices and medical devices incorporating, inter alia, substances which, if used separately, may be considered to be a medicinal substance within the meaning of Directive 65/65/EEC; whereas in such cases, if the substances incorporated in the medical devices are liable to act upon the body with action ancillary to that of the device, the placing of the devices on the market is governed by this Directive; whereas, in this context, the safety, quality and usefulness of the substances must be verified by analogy with the appropriate methods specified in Council Directive 75/318/EEC of 20 May 1975 on the approximation of the laws of the Member States relating to analytical, pharmaco-

[1] OJ No C 237, 12. 9. 1991 and OJ No C 251, 28. 9. 1992 p. 40.
[2] OJ No C 150, 31. 5. 1993 and OJ No C 176, 28. 6. 1993.
[3] OJ No C 79, 30. 3. 1992, p. 1.
[4] OJ No 22, 9. 6. 1965, p. 369/65. Directive as last amended by Directive 92/27/EEC (OJ No L 113, 30.4.1992, p. 8).

Page 1 of 49 pages

Target values

- Dose uniformity within ± 3%
- Lateral position precision of ± 0.5 mm
- Positioning precision of Bragg-peak: ± 0.3 mm

Example for safety measures:

Beam Application and Monitoring System (BAMS)

- Intensity verification (redundant)
- Lateral Position verification (redundant)
- Feed-back loop to achieve high precision and accuracy of beam application

Know How Transfer – from Research / Industry to Healthcare

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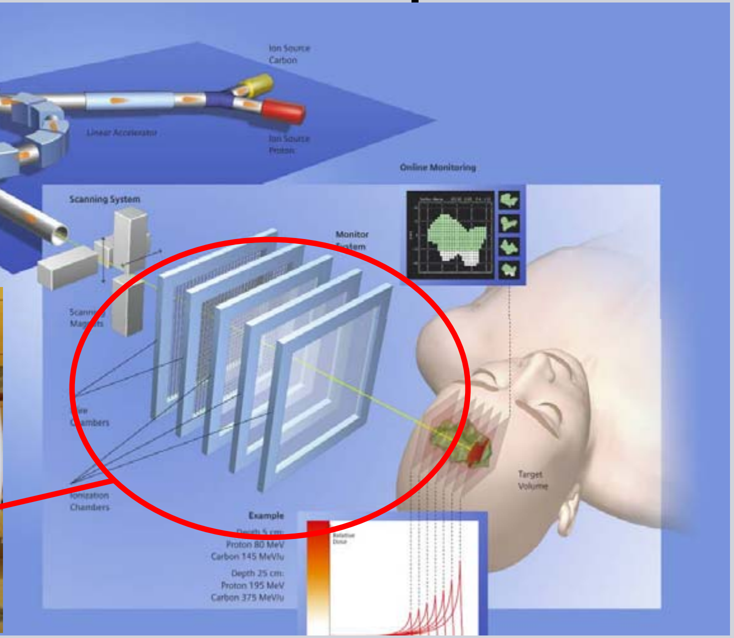
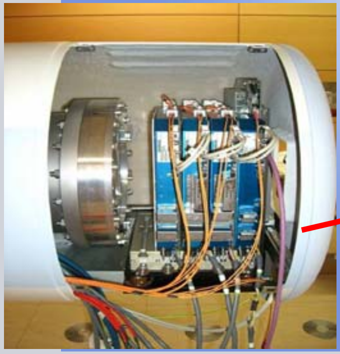
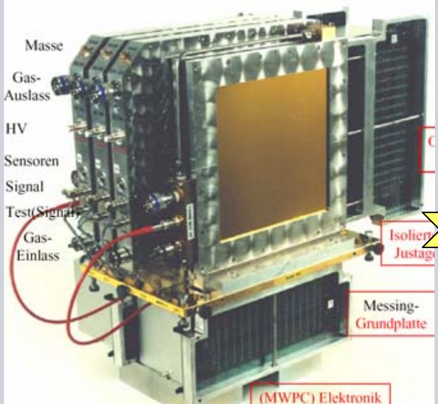
Example: Beam Application and Monitoring System (BAMS)

Based on GSI concept a detector system with highly integrated readout electronics has been developed

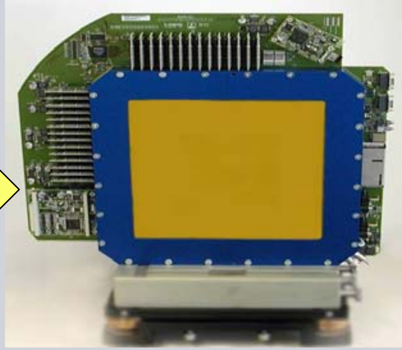




Beam Application and Monitoring System (BAMS)



Courtesy of GSI



- **Detector concept using ICs and MWPCs**
- **Fast dose & position measurement cycle**
- **High dynamic range :**
  - **10^6 – 10^{10} particles / s**
  - **50 MeV (p) – 430 MeV/u (C)**
- **Integrated readout electronics reusing existing hardware of other Siemens healthcare modalities**

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Market Players & Collaborations

What is the Background of the Market Players?

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Particle Therapy	Background	Radiation Therapy
IBA	Accelerator	Elekta (Cooperation)
Hitachi	Accelerator and Heavy Industry	-
Mitsubishi	Accelerator and Heavy Industry	-
Optivus	Operating of one PT Center (Loma Linda)	-
Siemens	Healthcare and Accelerator / Danfysik	Siemens
Sumitomo	Accelerator and Heavy Industry	-
Stillriver	Startup	-
Varian	Radiation Oncology and Accelerator / Accel	Varian
-	-	Accuray
-	-	Tomotherapy

Evolution and Market

From Research to Clinical Routine

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Clinical Application

Clinical Research

Fundamental Research

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Main R&D Topics
*What are the typical topics for **industry?***

- **Optimize cost and increase standardization**
- **Optimize integration into medical workflow**
- **Secure high uptime and technical operating as a long-term commitment over 20-25 years**
- **Provide financing models like Public Private Partnership (e.g. Kiel and Essen)**

Main R&D Topics

*What topics will remain with **Universities and Research Centers**?*

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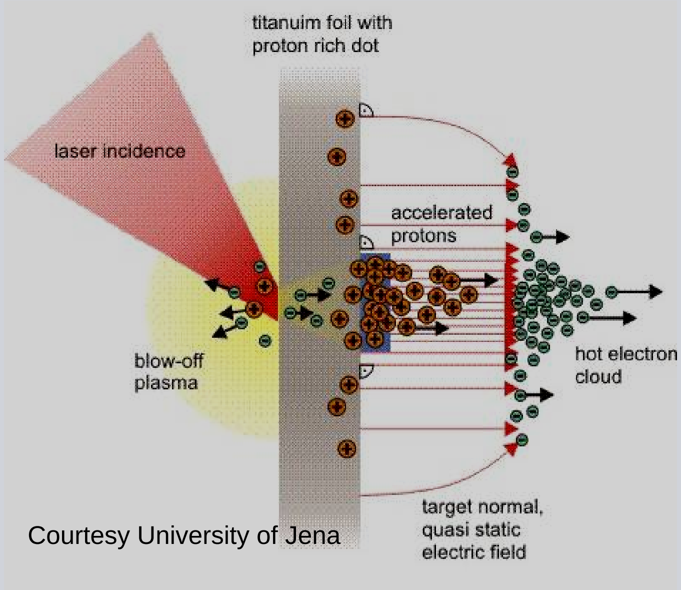
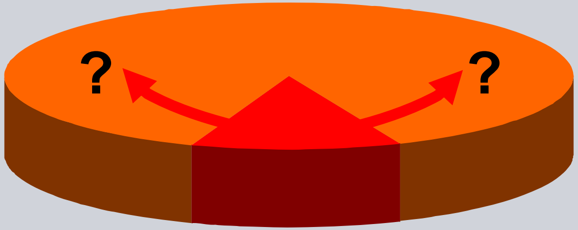
- **New Principles for Particle Accelerators**
  - **Laser Accelerated Particle Beams**
  - **Dielectric Wall Accelerators**
- **Radiation Biology**
  - **Radiobiological Models**
  - **Verification of Models**
- **New Clinical Applications**
  - **Moving Targets**
  - **Image Guidance**
  - **Hypofractionation**
- **Clinical Studies**
  - **Protocols for new cancer indications**



Courtesy University of Jena



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Careflow with an integrated future

Thank you for your attention

Siemens AG
Healthcare Sector
Particle Therapy