Brachytherapy:General Principles

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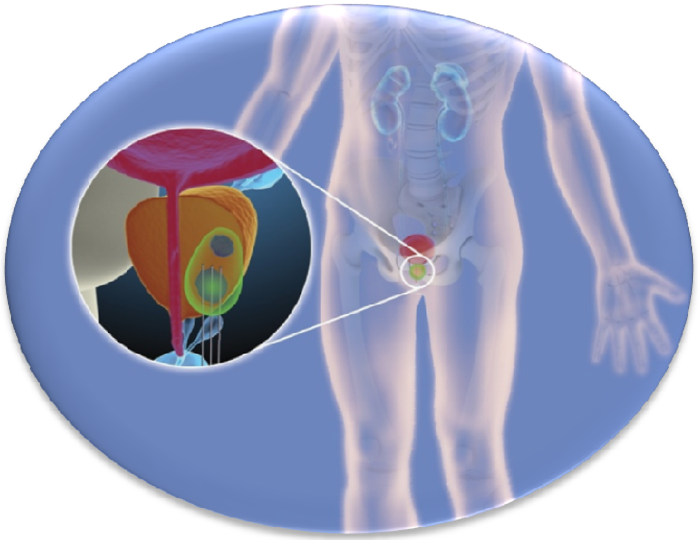
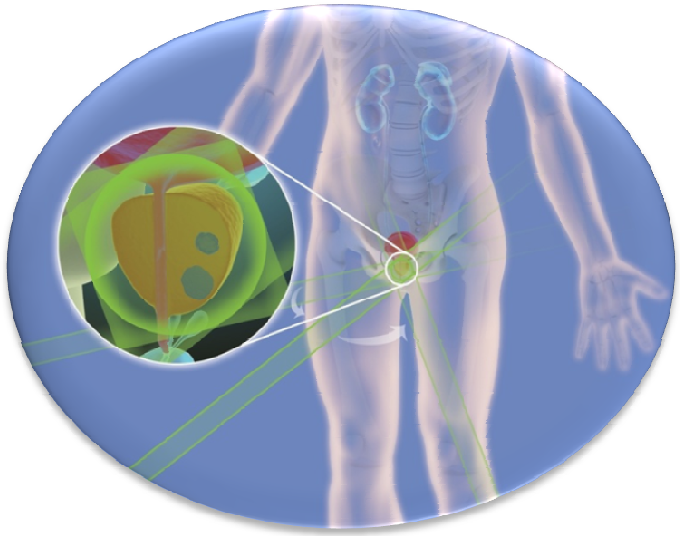
Brachytherapy:
The precise answer for tackling cancer

Derives from the Greek word 'brachy' – meaning short-distance
Brachytherapy involves placing small radiation sources internally, either into or immediately next to the tumor in a geometrical fashion , allowing precise radiation dose delivery[1] –
Treating the cancer 'from the inside, out'

Brachytherapy works 'from the inside, out'



EBRT works 'from the outside, in'



1. Stewart AJ & Jones B. In Devlin *Brachytherapy: Applications and techniques. 2*007.

Traditional EBRT and brachytherapy

	EBRT	Brachytherapy
Treated volume	Large	Small
Dose distribution	Homogenous	Heterogenous
Dose rate	High	Variable HDR, LDR, (PDR)
Fractionation	Multiple	Few
Treatment duration	Long; weeks to months	Short; hours to days

Adapted from Mazeron JJ, Scalliet P, Van Limbergen E *et al*. In: *The GEC ESTRO Handbook of Brachytherapy*. 2002.

Key concepts: Dose distribution

Unlike EBRT, brachytherapy is able to deliver a highly conformal dose at a high dose rate

Smaller volume + **Higher dose** =

Fewer fractions
- Short treatment
- Prevents repopulation of cancer cells
- Limits toxicity to surrounding tissue

Inverse Square Law

Gerbaulet A, Ash D, Meertems H *et al*. In *The GEC ESTRO handbook of brachytherapy*. 2002.

Brachytherapy:History

1896

- Radioactivity was described by Becquerel

1898

Marie curie extracted radium from pitchblende ore

1901

- Danlos and Bloc performed first radium implant (1901)

1931

The term brachytherapy proposed first time by Forsell

1940-1970s

Co^{60},Ta^{182}, Cs^{137}, Ir^{192} first used in brachytherapy

Cs^{137} began to replace Ra^{226}

1953

- Aterloading technique first introduced by Henschke in New York – removed hazard of radiation exposure. Also Ir-192 used first time by Henschke

Brachytherapy:History

1940-50

Brachytherapy rules were developed and followed

1953

LDR brachytherapy became the gold standard

1968

- HDR brachytherapy was introduced

1950s and 1960s

- New radioactive sources, techniques and equipment, which prevented unnecessary radiation exposure to patients and clinicians led to a renaissance for brachytherapy[1]

1970s

- Brachytherapy is established as a safe and effective standard of care for many gynecological cancers[5]

Present day

- Brachytherapy a valued treatment option for many types of cancer, with a wealth of supporting evidence[4,5] with maqny advances.

1. Gupta VK. *J Medical Physics* 1995;20(2):31-5. 2. Nag S. American Brachytherapy Society.
3. Aronowitz JN, Aronowitz SV Robison RF. *Brachyther* 2007;6:293-7. 4. Blasko JC, Wallner K, Grimm PD *et al. J Urol* 1995;154:1096-9.
5. Viani GA, Manta GB, Stefano EJ *et al*. *J Exp Clin Cancer Res* 2009;28:47.

History of Brachytherapy

Rules for implantation were made for LDR

Interstitial Brachytherapy:

- Manchester system
- Quimby System
- Memorial System
- Paris system

Surface Mould

- Manchester system

Intracavitary Brachytherapy:

- Stockholm system (1914)
- Paris System (1926)
- Manchester System (1938)

Last 4 decades have seen the emergence of remote after loading system (selectron machine – LDR machine – first time used in 1970 for ca cx)

HDR became widely accepted after a long struggle in early 90's

PDR has been developed

Now with more sophisticated imaging, hardware and software : image based and image guided brachytherapy has come up.

Advantages

1. ***High dose* of radiation is delivered to *tumor* in short time. So biologically very effective**
2. ***Normal tissue* spared due to rapid dose fall off**
3. **Better tumor control**
4. **Radiation morbidity minimal**
5. **Cosmetic superiority over teletherapy**
6. **Acute reactions appear when treatment is over; so no treatment breaks. Also radiation reactions localized & manageable**
7. ***Treatment time* short – reduces risk of tumor repopulation**
8. **Therapeutic ratio high**
9. **Also decreased burden on patient & family**

Limitations

1. **Applicable to *accessible* sites only**

2. **Application limited to *small size* tumors (T1 , T2)**

Disadvantages

1. **Invasive procedure**
2. ***Radiation hazard* due to radioisotopes (in olden days due to preloading techniques, now risk decreased)**
3. **General anesthesia required**
4. **Dose inhomogeneity is higher than EBRT (but acceptable if rules followed)**
5. **Because of greater conformity, small errors in source placement can lead to extreme changes from the intended dose distribution**
6. **Present day brachytherapy is costly**

Types of brachytherapy

Classification schemes:
1. depending on use/radionuclide position
2. depending on loading pattern
3. depending on duration of irradiation
4. depending on dose rate

Types of Brachytherapy……

- **Depending on use** (surgical approach to target volume)

o Source in contact with but superficial to tumor:

surface moulds

o Source inside the tumor/target

- Interstitial
- Intracavitary
- Intraluminal
- Intravascular

- **Surface dose applications** (plesiocurie/mold therapy)

  consists of an applicator containing array of radioactive sources designed to deliver a uniform dose distribution to skin/mucosal surface
- **Interstitial brachytherapy**

  surgically implanting small radioactive sources directly into target tissues
- **Intracavitary brachytherapy**

  consists of positioning applicators bearing radioactive sources into the body cavity in close proximity to target tissue
- **Transluminal brachytherapy**

  consists of inserting single line source into a body lumen to treat its surface &adjacent tissue
- **Intravascular brachytherapy**

Types of Brachytherapy……

- **Depending on source loading pattern:**
  - *Preloaded:* **inserting needles/tubes containing radioactive material directly into the tumor**
  - *After loaded:* **first, the non-radioactive tubes inserted into tumor**
    - **Manual: Ir^{192} wires, sources manipulated into applicator by means of forceps & hand-held tools**
    - **Computerized remote controlled after loaded: consists of pneumatically or motor-driven source transport system**

Preloading pattern

- **Advantage:**
  - Loose & flexible system(can be inserted even in distorted cervix)
  - Excellent clinical result
  - Cheap
  - Long term results with least morbidity (due to LDR)

- **Disadvantages:**
  - Hasty application -Improper geometry in dose distribution
  - Loose system – high chance of slipping of applicators – improper geometry
  - Application needed special instruments to maintain distance.
  - Radiation hazard
  - Optimization not possible

After loading pattern

MANUAL AFTERLOADING

Advantages

1. Circumvents radiation protection problems of preloading
2. Allows better applicator placement and verification prior to source placement.
3. Radiation hazard can be minimized in the OT / bystanders as patient loaded in ward.
4. Advantages of preloading remain as practised at LDR.

Disadvantages:

specialized applicators are required.

APPLICATORS

Gynae Applicators

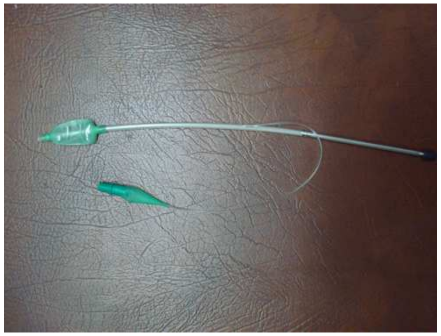
Vaginal Sorbo

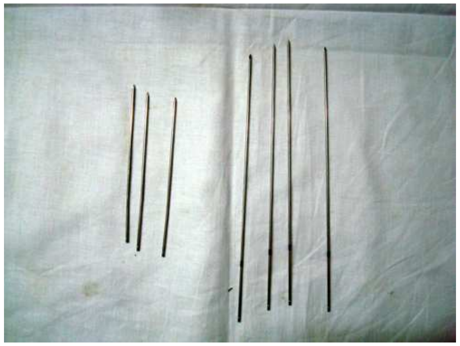
Esophageal Bougie

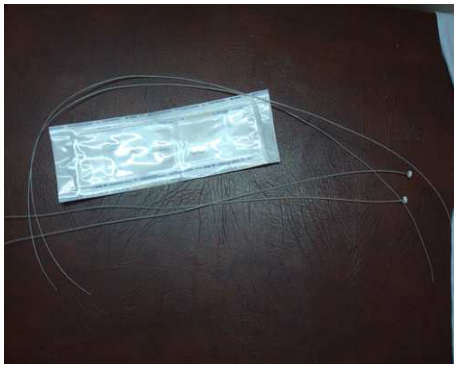
Nasopharyngeal Applicator

Steel Needles

Plastic Catheters & Buttons







REMOTE AFTERLOADING

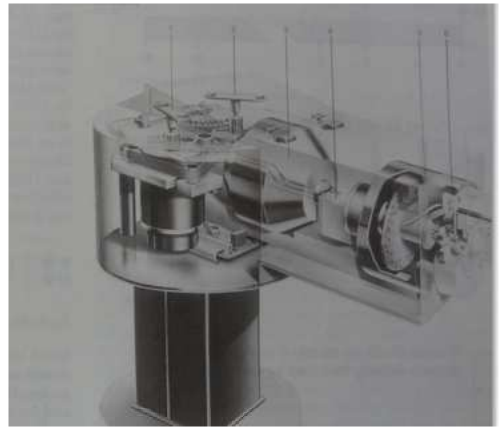
Advantages :

1. **No radiation hazard**
2. **Accurate applicator placement**
   - **-ideal geometry maintained**
   - **-dose homogeneity achieved**
   - **-better dose distribution**
3. **Information on source positions available**
4. **Individualization & optimization of treatment possible**
5. **Higher precision , better control**
6. **Decreased treatment time- opd treatment possible**
7. **Chances of source loss nil .**

Disadvantages :

1. **costly**
2. **Still some grey areas in dose conversions**

Afterloading Systems



Microselectron,Varies Source & Gammamed

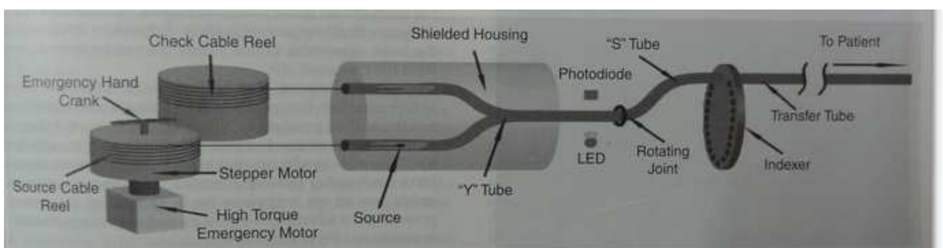


FIGURE 21.2. Components of a high dose-rate brachytherapy remote afterloader. (Figure by Adam Uselmann after the draft by Liyong Lin).

Selectron MDR

Types of Brachytherapy……

Depending on Dose-Rate used

Acc. To ICRU REPORT no.38 :

- *Low dose rate (LDR):* **0.4-2 Gy/hour**
  Hours to days- Confinement to bed
  LDR A/L: 1970s using Cs^{137}

- *Medium dose rate (MDR):* **2-12 Gy/hour**
  in Mid 70s Cs137-

- *High dose rate (HDR):* **>12 Gy/hour (0.2 Gy/min)**
  1st in 1968-joslin (cathetron)
  1984-PGI
  (Co^{60} source drawn to high intensity)

- *Ultra-low dose rate (ULDR):* **0.01-0.3 Gy/hour**

- **ROUGHLY**
  - **LDR – 10 Gy/day**
  - **MDR -10 Gy/hr**
  - **HDR – 10 Gy/min**

LDR-advantages

1. ***Clinical effects* –predictable**
   -large body of data spanning 4-5 decades
   -experience with various radionuclides
2. ***Radiobiologically* superior**
   -allows continous radiation to tumor as well as simultaneous repair of sublethal damage in normal tissues
3. **Long *experience***
   -well defined rules for use exist which allow optimum implant dosimetry
4. **Less morbidity & best tumor control**
5. **Cheap**
6. **Since 1-2 sessions required**
   -intersession variability in dose distribution minimized

LDR-disadvantages

1. **Treatment continuous and prolonged.**

   -confined to bed

2. **Geometry and distribution not properly maintained**

3. **Limited applicability in elderly patients, with respiratory, cardiac problems**

4. **Individualization & optimization not possible**

MDR

ADVANTAGES :

1. treatment completed in shorter treatment time
2. increased patient convenience
3. considered radiobiologically nearer to LDR brachytherapy

DISADVANTAGES :

1. without correction, increased incidence of late complication (20 – 30 %)
2. few results despite widespread use at one time

HDR-advantage

1. **Shorter treatment times, resulting in:**
   a) OPD based treatment possible
   b) Less patient discomfort
      (prolonged bed rest is eliminated)
   c) Reduced applicator movement during
      therapy(geometry well maintained)
   d) Greater displacement of nearby normal tissues.
   e) Possibility of treating larger number of patients

2. **Allows use of smaller & thinner applicators than are used in LDR:**
   a) **Resulting in lesser tissue trauma**
   b) **Reducing the need for dilatation of the cervix and therefore reducing the need for heavy sedation or general anesthesia (allowing treatment for high-risk patients who are unable to tolerate general anesthesia).**
   c) **Geometrical sparing can circumvent radio biological disadvantage**

3. **Tailor dose distribution to target through *optimization* due to stepping source technique used.**

4. ***Elimination of exposure* to personnel**

HDR-disadvantages

1. **Decreased therapeutic ratio**

   -short treatment time-doesn't allow repair of sublethal damage to normal tissues and redistribution & reoxygenation of tumor cells(radiobiologically inferior as normal tissue becomes more sensitive)

2. **Multiple sessions**

   -different geometry each time

3. **Less time to detect & correct error**
4. **Limited experience**

   -till recently, no standard guidelines

5. **Economic disadvantage**

   -Labour intensive

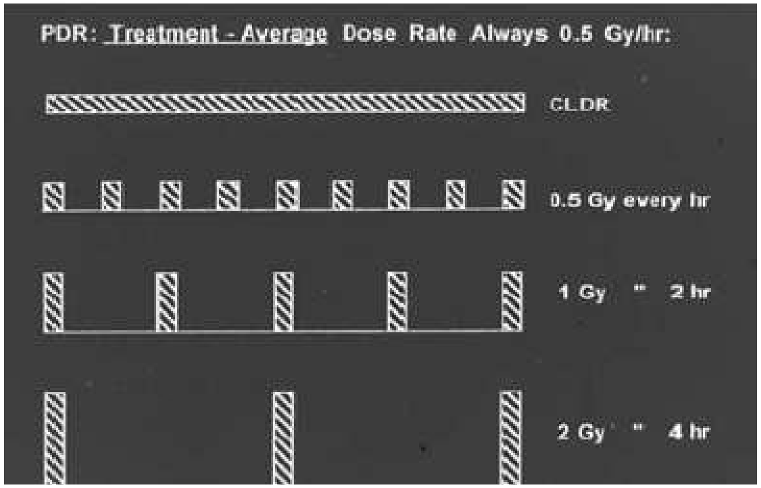
   -large capital investment

PDR Brachytherapy

- **Series of short HDR treatments (10 minute pulse repeated at 1 hr intervals) replacing the continuous LDR treatment lasting several days- PDR BT.**
- **Overall time remains same as LDR**
- **Source strength : 1 Ci**
- **ADVANTAGE:**

radiobiologically nearer to LDR

optimization possible



Types of Brachytherapy……

- **Depending upon means of controlling dose delivered(duration of irradiation)**
  - **Temporary/Removable implants**

    when the radioactive source implanted into the tumor tissue is allowed to remain there for definite period . Ex Cs^{137}, Ir^{192}
  - **Permanent implants**

    when the sources are implanted indefinitely ex: Pd^{103}, Au^{198}

These terms used for interstitial form of brachytherapy

Permanent implant

Advantages :

1. Useful for less accessible sites (e.g. prostate, endovascular)
2. Allows a continuous ultra-low dose rate treatment (maximum biological effectiveness)
3. Allows better normal tissue healing due to low dose rate
4. Cell kill predominantly by alpha damage (KeV photons , PE effect)– better efficacy in slow growing and radio-resistant tumors.
5. Patient mobility maintained after procedure

Disadvantages :

1. Radiation protection issues in case of source being excreted (e.g. urine)
2. Dosimetry uncertain due to short half life – latter part of treatment becomes progressively less effective
3. Source migrations known to occur – resultant perturbation in dose distributions
4. Sources expensive – can’t be reused.
5. Complicated implant procedure – difficult to maintain geometry esp. for larger tumors.
6. Radiobiologically inferior in rapidly proliferating tumors

Radioactive sources

- ***Obsolete or historical***

  ^{226}Ra, ^{222}Rn

- **Currently used sealed sources**

  ^{137}Cs, ^{192}Ir, ^{60}Co, ^{125}I, ^{103}Pd, ^{198}Au, ^{90}Sr.

- **Developmental sealed sources**

  ^{241}Am, ^{169}Yb, ^{252}Cf, ^{131}Cs, ^{145}Sm.

Characteristics of a radioisotope

- **Half life-**

  Time required for the activity of the source to decay to half the initial value.
- **Gamma energy**
- **Specific activity-**

  Activity per unit mass of a radio nuclide.(Ci/gm)
- **Half value layer-**

  Thickness of the material required to decrease the intensity of the incident beam to half of it original value
- **Exposure rate constant- Gamma ray constant**

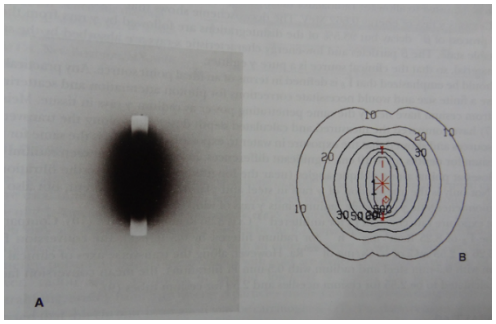
  Defined as the exposure in R/hr at a point 1 cm from a 1 mCi point source.(R cm^2/hr/mCi)
- **Beta Energy& filtration**

What is an Ideal Radionuclide?

- **Easily available & Cost effective**
- **Gamma ray energy high enough to avoid increased energy deposition in bone by PEE & low enough to minimise radiation protection requirements**
  - **Preferably monoenergetic: Optimum 300 KeV to 400 KeV(max=600 kev)**
- **Absence of charged particle emission or it should be easily screened (Beta energy as low as possible: filtration)**
- **Half life such that correction for decay during treatment is minimal**
  - **Moderate (few years) T1/2 for removable implants**
  - **Shorter T1/2 for permanent implants**
- **Moderate gamma ray constant (determines activity & output) & also determine shielding required.**

What is an Ideal Radionuclide?

- **No daughter product;** No gaseous disintegration product to prevent physical damage to source and to avoid source contamination
- **High Specific Activity (Ci/gm)** to allow fabrication of smaller sources & to achieve higher output (adequate photon yield)
- **Material available** is insoluble & non-toxic form
- **Sources can be made in** different shapes & sizes: Tubes, needle, wire, rod, beads etc.
- **Should withstand sterilization process**
- **Disposable without** radiation hazard to environment
- **Isotropic:** same magnitude in all directions
- around the source
- **No self attenuation**



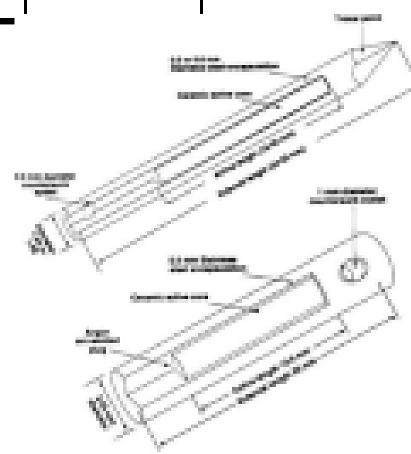
Why Ra not used now?

- **Spectrum has >8 photon energies ranging from 0.047-2.45 MeV : gives heterogenous beam & non uniform dose distribution**
- **Low specific activity : 1 Ci/gm : large dia of needles will be needed**
- **High gamma ray constant: requires more protection**
- **High energy: large HVL reqd :high radiation shielding will be reqd**
- **Rn 222 being the gaseous daughter product-threat of leaks especialy from long bent needles(long t1/2)**
- **Storage & disposal of leaked sources a big problem**
- **Ra source costly**

RADIUM SUBSTITUTES

- **Currently used sealed sources**

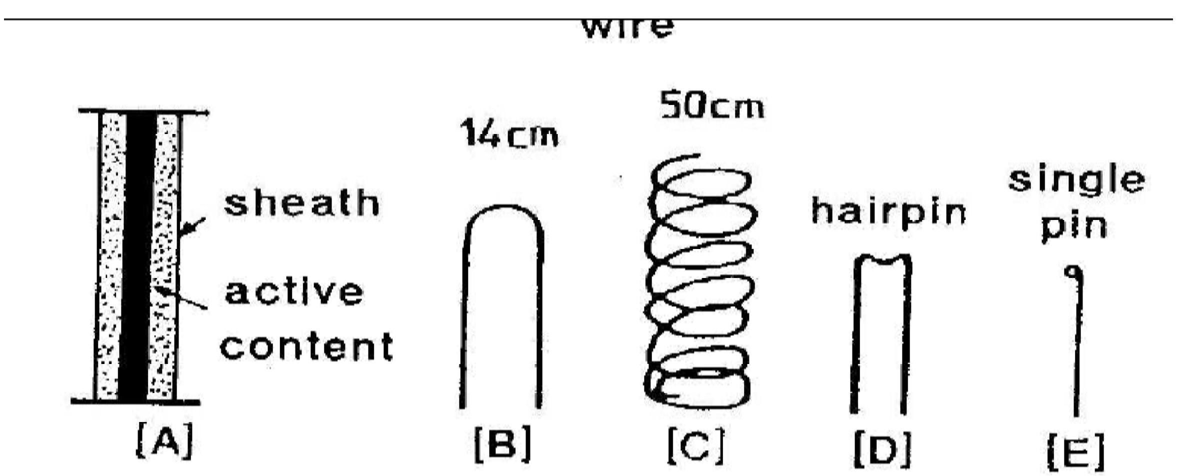
Element	Energy (MeV)	Half-life	HVL-Lead (mm)	Exposure rate constant	Source Form	Clinical application
Cesium Cs^{137}	0.662	30 yrs	6.5	3.28	Tubes & Needles	LDR I/C &temporary Implants
Cobalt Co^{60}	1.25 average	5.26 yrs	11	13.07	Encapsulated spheres	HDR I/C

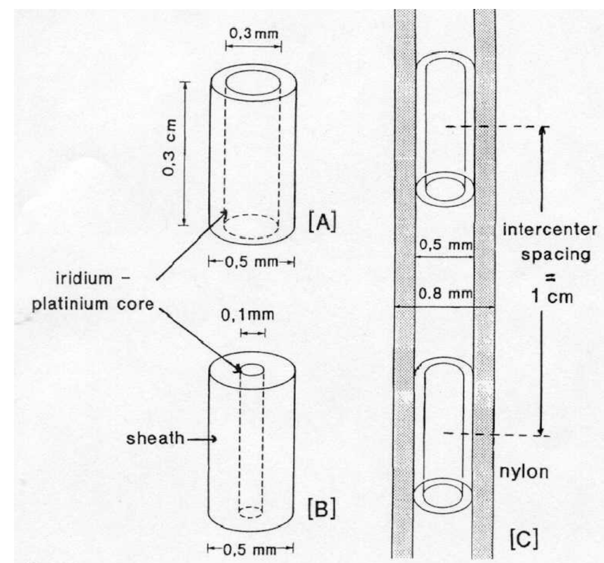


Cesium or Cobalt needles,Tubes & Pallets

- **Currently used sealed sources**

Element	Energy (MeV)	Half-life	HVL-Lead (mm)	Exposure rate constant	Source Form	Clinical application
Iridium Ir^{192}	0.397 average	73.8 days	6	4.69	Seeds in nylon ribbons; Metal wires; Encapsulated source on cable	LDR & HDR temporary implants HDR I/C Intravascular





Ir-192 near ideal radioisotope?

- Compatible with after loading techniques
- Ideal energy (0.3 – 0.4 Mev) – monoenergetic – more radiobiological effect
- Flexible & malleable – can be used in form of wires of any size
- Energy is low – thinner shields reqd for radiation safety
- β energy is low – so lesser filtration reqd
- No products
- Easily available, less costly

Limitation

Short half life so source has to be replaced every 3 months

- **Currently used Seed sources**

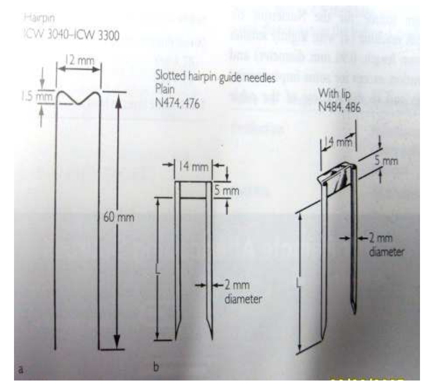
Element	Energy (MeV)	Half-life	HVL-Lead (mm)	Exposure rate constant	Source Form	Clinical application
Gold Au^{198}	0.412	2.7 days	6	2.35	Seeds	Permanent Implants
Iodine I^{125}	0.028	59.6 days	0.025	1.45	Seeds	Permanent Implants
Palladium Pd^{103}	0.020	17 days	0.013	1.48	Seeds	Permanent Implants

Newer Isotopes

Name	$T_{1/2}$	Photon energy (KeV)	10^{th} VL	Comment
Samarium 125	340 days	41	0.2	Sensitization of cells to radiation damage by iodinated deoxyuridine due to photon energy
Americium 241	432 yrs	60	0.42	Low specific activity and α emitter
Ytterbium 169	32 days	93	1.6	Highest specific activity and lower tissue attenuation
Californium 252	2.65 yrs	NA	NA	Neutron emitter used in brachytherapy and as EBRT source. 2.3×10^9 / sec (neutrons)

SOURCE FORMS

- Needle
- Tube
- Wire
- Hair pin
- Cylinder
- spherical
- Beads
- Pellets
- Micro pellets



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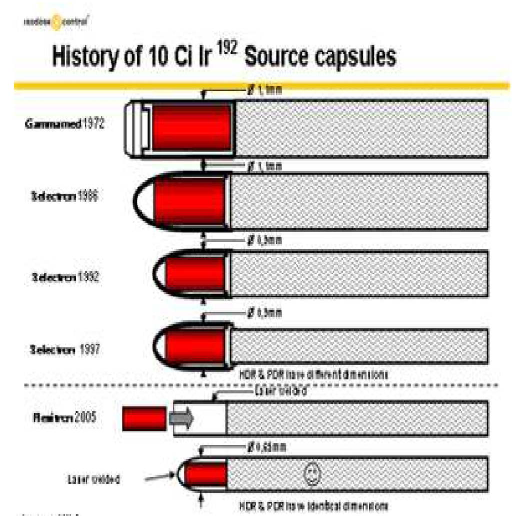


Radio-isotopes Used in Radiotherapy and their Physical Charactrestics

Sr. No.	Radio-Isotope	γ-Energy (MeV)	β- Energy (MeV)	Gamma Constant	Half Lfie	HVL (Pb)	Form	Use
1.	Ra-226	0.047-2.44	0.017.3.26	8.25 R	1620 yrs.	1.4	Needles, tubes	I/C,Mou ld,Ints.
2.	Rn-222	0.047-2.44	0.017-3.26	8.25 R	3.8 yrs.	1.2	Seeds	Ints.
3.	Tn-182	0.043-1.45	0.18-0.514	6.71R	115 days	1.2	Wires, pins, ribbon	Ints.
4.	Co-60	1.17-1.33	0.313	13.25R	5.2 yrs.	1.2	Needles, tubes, teletherapy sources	I/C, Mould, Ints. ,I/L
5.	Cs-137	0.33	0.52-1.17	3.22 R	30 yrs	0.65	Needles, tubes, pallets	-do-
6.	Ir-192	0.3.06	0.24-0.67	4.62 R	74.2 days	0.30	Wires, seeds, ribbons	-do-
7.	I-125	0.035	None	1.20 R	60.2 days	0.0	Seeds	Ints.
8.	An-198	0.4-1.08	0.96	2.32 R	2.7 days	0.33	Seeds	Ints.
9.	P-32	None	1.71	--	14.3 days	0.01	Plaques	I/V Stent

I/C – Intracavitary, Ints. – Interstitial , I/L – Intraluminal , I/V – Intra-vascular

Radio-isotopes Used in Radiotherapy and their Physical Chractrestics

Sr. No.	Radio-Isotope	γ-Energy (MeV)	β -Energy (MeV)	Gamma Constant	Half Lfie	HVL (Pb)	Form	Use
10.	Sr-90	None	0.54.2.27	--	28.9 yrs	0.01	Plaques	Plaque
11.	Cr-252	1.5 & 1.0 Neutron 2.1 & 2.3	--	--	54 yrs	--	Tubes	I/C
12.	Pd-103	0.21 (mean) 0.02-0.497	--	--	17 days	0.03 mm	Seeds	Ints.
13.	Sm-145	0.041 (mean) 0.038-0.061	--	--	340 days	0.2 mm	--	-do-
14.	Am-241	0.060 (mean) 0.014-0.059	--	--	432 days	0.42 mm	--	-do-
15.	Yt-169	0.093 (mean) 0.050-0.0307	--	--	32 days	3.3 mm	--	-do-

I/C – Intracavitary, Ints. – Interstitial , I/L – Intraluminal , I/V – Intra-vascular

Source Strength Specification: Quantities and Units

Quantity and Units :-

1. mg Radium or mg radium equivalent.
2. mg hours
3. Roentzen
4. Rads or Centigray

Activity :-

1. Curie or mCi
2. Air kerma strength

Dose Calculations :-

1. Lane's approximation
2. Sievert integral
3. Computer dose calculations.

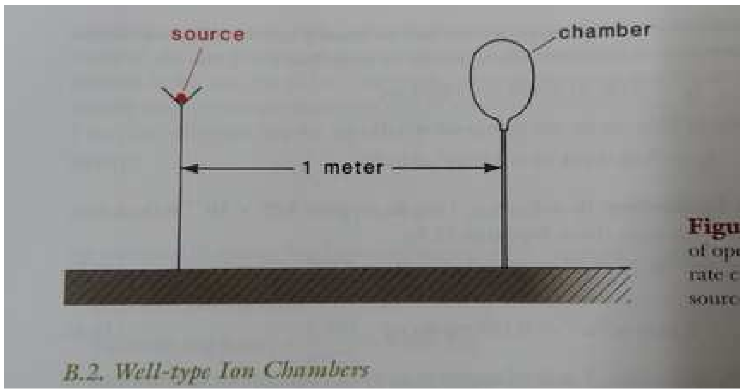
Radiation Safety

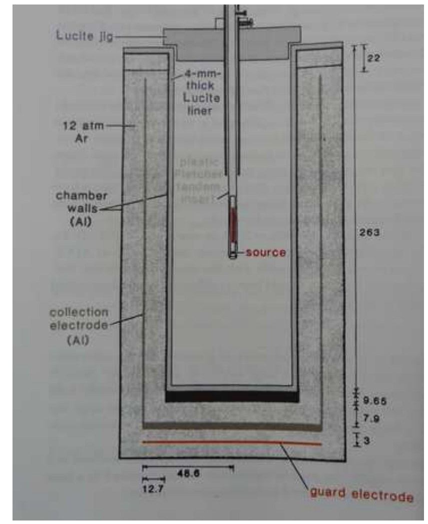
Radiation Shield

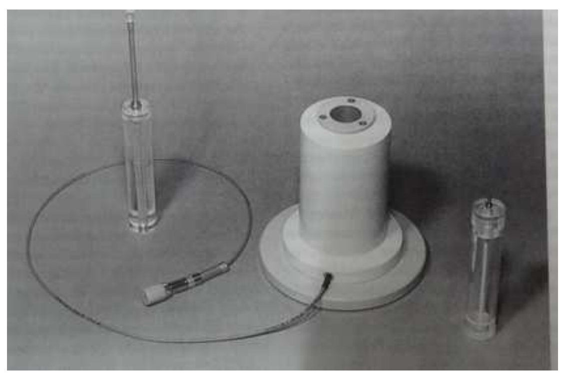
Radio-isotop

Calibration of Sources

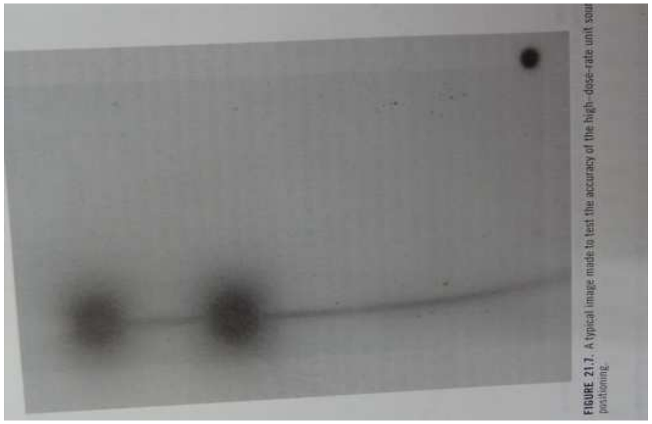
Well Type Chamber



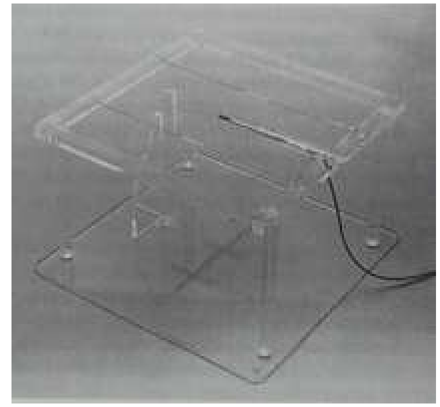


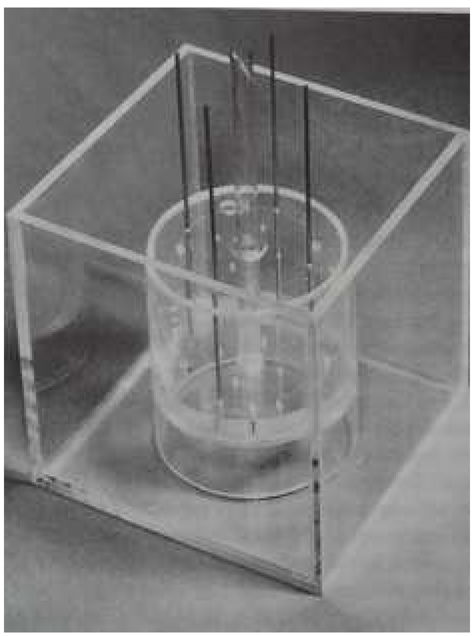


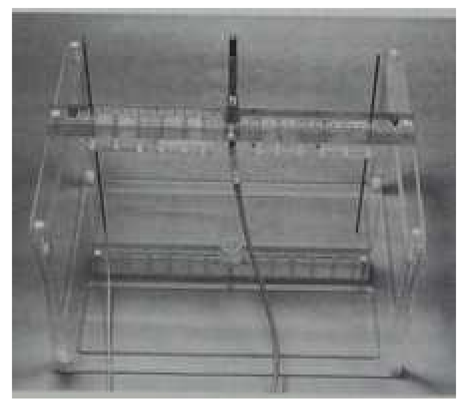
Calibration of Sources



Zigs







Clinical criteria for brachytherapy

1. ***Small size*** **tumors (3 – 5 cm)**
2. **Depth of penetration/thickness < 1.5 – 2 cm**
3. **Histology: moderately *radiosensitive* tumors (ca squamous cell);some adenocarcinomas**
4. ***Early stage*** **(localized to organ)**
5. **No nodal/distant metastasis**
6. **Location : *accessible* site with relatively maintained anatomy**
7. **Absence of local infection & inflammation**

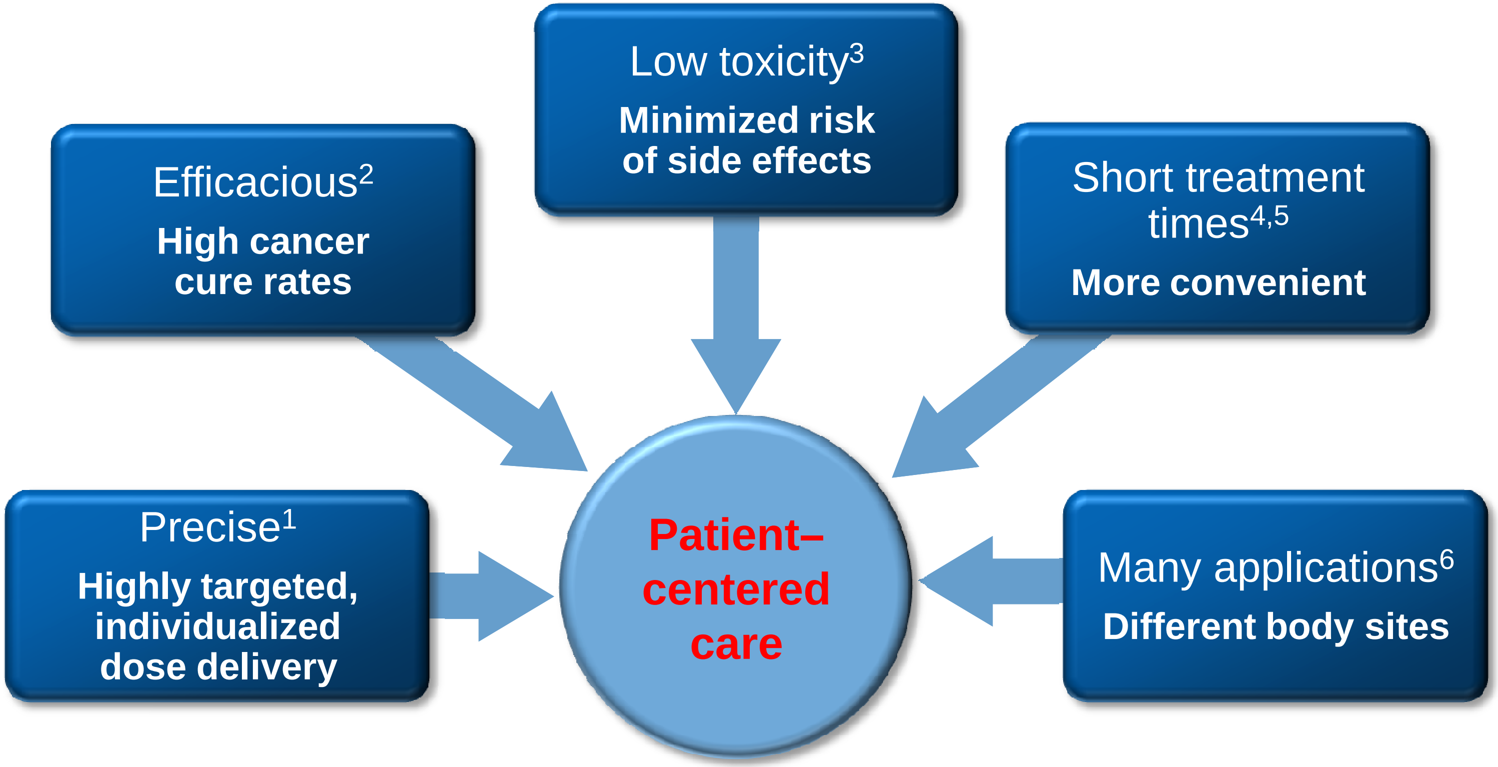
Indications

- **For radical radiation alone:**
  - Skin tumors
  - Head and Neck cancer – Oral Cavity
  - Cervical cancer
  - Prostate cancer
  - Penile cancers
  - Ocular tumors
  - Breast cancer
- **As a boost after EBRT ± Chemotherapy:**
  - Head and neck cancers – Oral Cancer
  - Cervical cancers
  - Breast cancer
  - Esophagus
  - Anal canal

Indications

- **In the post-operative setting:**
  - **Perioperative:**
    - **Soft tissue sarcomas**
    - **Breast**
  - **Postoperative:**
    - **Endometrium**
    - **Cervix**
    - **Breast**
- **Palliative setting:**
  - **Bronchus**
  - **Bile ducts**
  - **Selected esophagus**
  - **Selected recurrent tumors (chest wall , head and neck)**
- **Benign tumors:**
  - **Keloids**
  - **Pterygium**
- **Other indication:**
  - **Endovascular brachytherapy**
  - **Radioactive stents**

Brachytherapy meeting patient's needs



Brachytherapy offers a precise, highly effective and well tolerated treatment option tailored to the needs of individual patients

1. Stewart AJ & Jones B. In Devlin. *Brachytherapy: Applications and Techniques*. 2007. 2. Kupelian PA, Potters L, Khuntia D, *et al. Int J Radiat Oncol Biol Phys* 2004;58(1):25-33. 3. Pisansky TM, Gold DG, Furutani KM, *et al. Mayo Clin Proc* 2008;83(12):1364-72. 4. Dickler A, Patel RR, Wazer D. *Expert Rev Med Devices* 2009;6(3):325-33. 5. Viani GA, Manta GB, Stefano EJ, *et al. J Exp Clin Cancer Res* 2009;28:47. 6. Sylvester JE, Grimm PD, Blasko JC*, et al. Int J Radiat Oncol Biol Phys* 2007;67(1):57-64.

Brachytherapy: Incorporating advanced imaging and computing technology into planning and treatment

2D Film – Based[1]

Standardization through protocols – Paris system

(e.g. breast) and Manchester method (gyn)

3D Volume – Based[2]

Dose/volume optimization with availability of 3D imaging capabilities

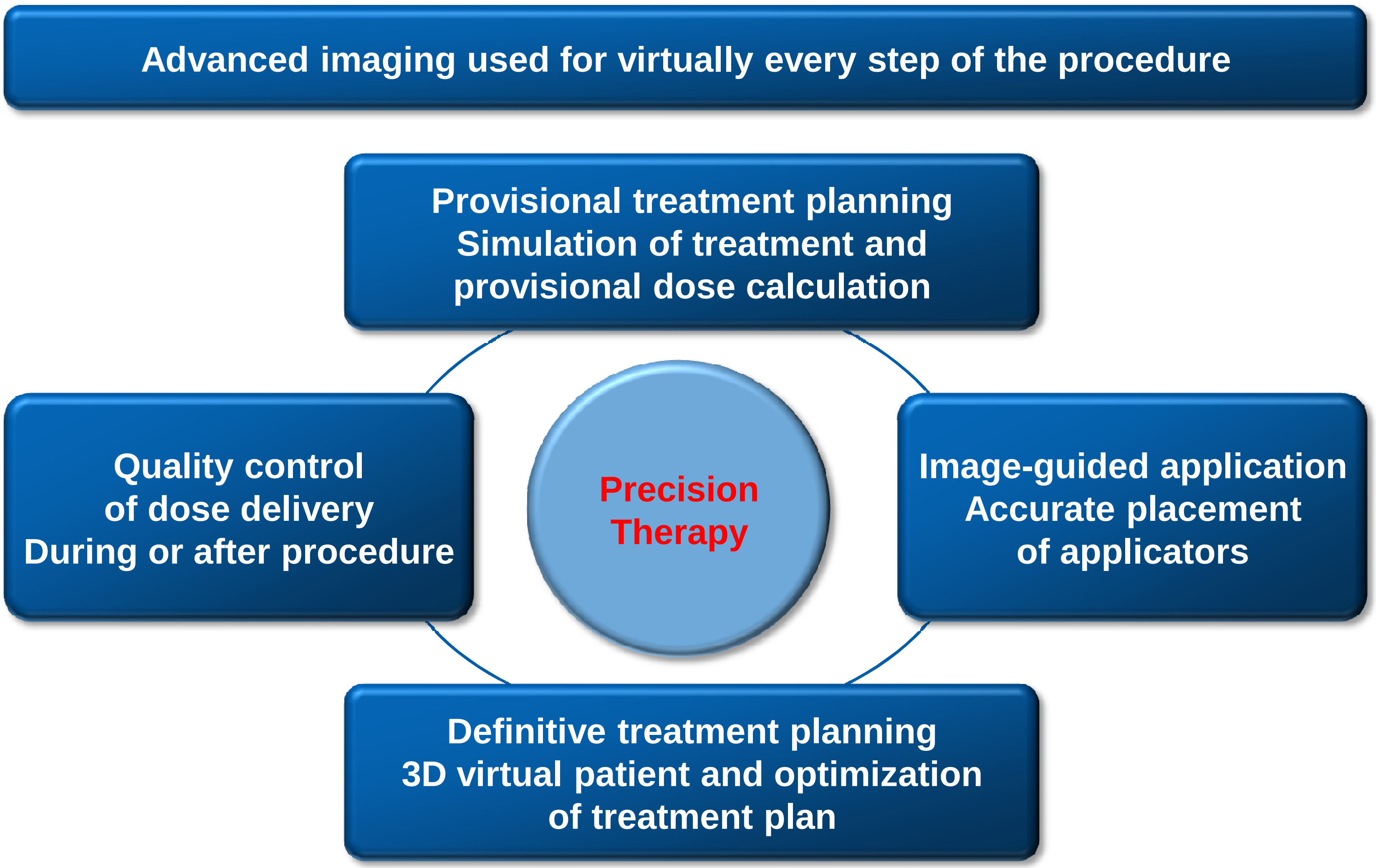
(CT/MRI)

Dynamic (real-time) dose based placement guidance

Image-guided adaptive brachytherapy

1. Meertens H, Briot E. In *The GEC ESTRO handbook of brachytherapy.* 2002.
2. Hoskin PJ & Bownes P. *Semin Radiat Oncol* 2006;16(4):209-17.

Image-guided planning and delivery



Gerbaulet A, Ash D, Meertems H *et al*. In *The GEC ESTRO handbook of brachytherapy.* 2002.

Delivering precision treatment

Brachytherapy delivers targeted radiation through the combination of computer-based planning, imagery and treatment delivery techniques via specialized applicators

Imaging

Clinical examination and tumor imaging

Application insertion

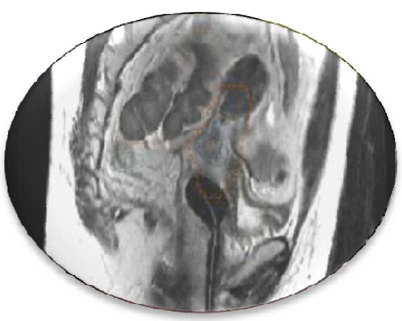
Source applicators placed in body for accurate positioning

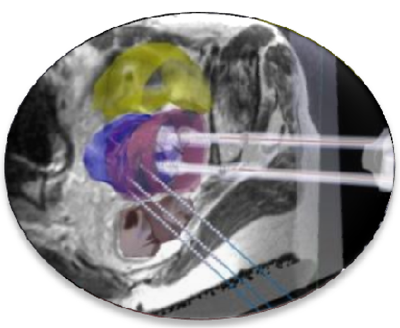
Optimizing treatment plan

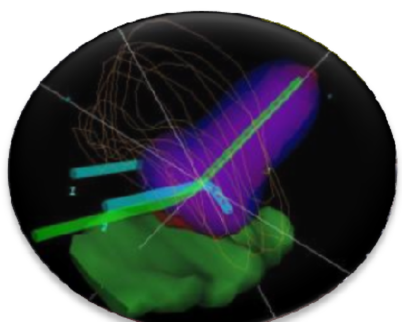
Create virtual patient via visualization and refine

Delivery

Sources delivered to treatment site via applicators







Brachytherapy-A multidisciplinary approach

Thank You