

# Compact Accelerator based Neutron Sources and the IAEA

Ian Swainson, Haifa Ben Abdelouahed, Sotirios Charisopoulos, Kalliopi Kanaki, Milan Matos, Danas Ridikas, Natko Skukan

**Physics Section, IAEA** 

### Considerations around a (first) Research Reactor

- Build the legal and regulatory framework in the country
- Obtain operating experience with aim of supporting eventual nuclear power program
- Build overall technical capacity in the country
- National pride
- Isotope production
- Research possibilities with neutrons

- Public opposition
- Capital expense
- Fuel security (suppliers)
- Physical security
- High level nuclear waste
- Decommissioning expense

# Considerations around a (first) CANS

- Build the legal and regulatory framework in the country
- Obtain operating experience with aim of supporting eventual nuclear power program
- Build overall technical capacity in the country
- National pride
- Isotope production
- Research possibilities with neutrons

- Public opposition
- Capital expense
- Fuel security (suppliers)
- Physical security
- High level nuclear waste
- Decommissioning expense

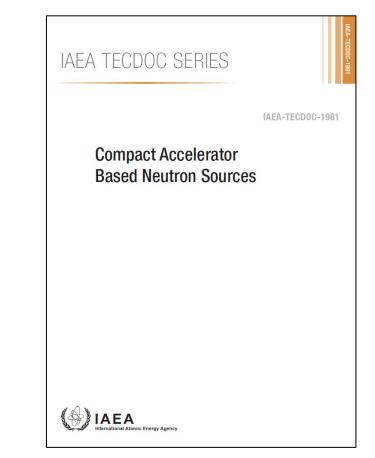






# Technical Meeting on non-spallation neutron production

- The output in 2021 was an IAEA report on CANS (the first one ever)
- The intent was to provide an overview of accelerator technologies, choices, costing, regulatory outlook etc.
- And to provide a document that can be cited during proposals for CANS.



https://www-pub.iaea.org/MTCD/publications/PDF/TE-1981web.pdf A very few printed copies available

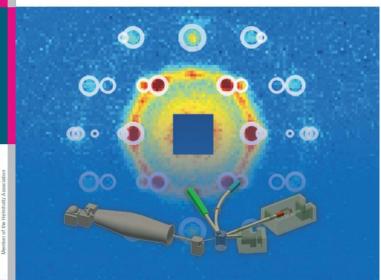
#### Neutron scattering sources

#### **Conceptual Design Report**

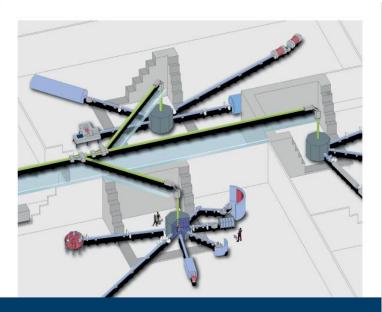
NOVA ERA (Neutrons Obtained Via Accelerator for Education and Research Activities) A Jülich High Brilliance Neutron Source project



Eric Mauerhofer, Ulrich Rücker, Tobias Cronert, Paul Zakalek, Johannes Baggemann, Paul-Emmanuel Doege, Jingjing Li, Sarah Böhm, Harald Kleines, Thomas Gutberlet, and Thomas Brückel



- Two example CDRs developed by FZ Julich
- Local source for a university based around commercial electrostatic accelerator
- National neutron source to "replace" RR based around highcurrent linac.



#### Conceptual Design Report Jülich High Brilliance Neutron Source (HBS) T. Brückel, T. Gutberlet (Eds.)

J. Baggemann, S. Böhm, P. Doege, J. Fenske, M. Feygenson, A. Glavic, O. Holderer, S. Jaksch, M. Jentschel, S. Kleefisch, H. Kleines, J. Li, K. Lieutenant, P. Mastinu, E. Mauerhofer, O. Meusel, S. Pasini, H. Podlech, M. Rimmler, U. Rücker, T. Schrader, W. Schweika, M. Strobl, E. Vezhlev, J. Voigt, P. Zakalek, O. Zimmer

Allgemeines / General Band / Volume 8 ISBN 978-3-95806-501-7

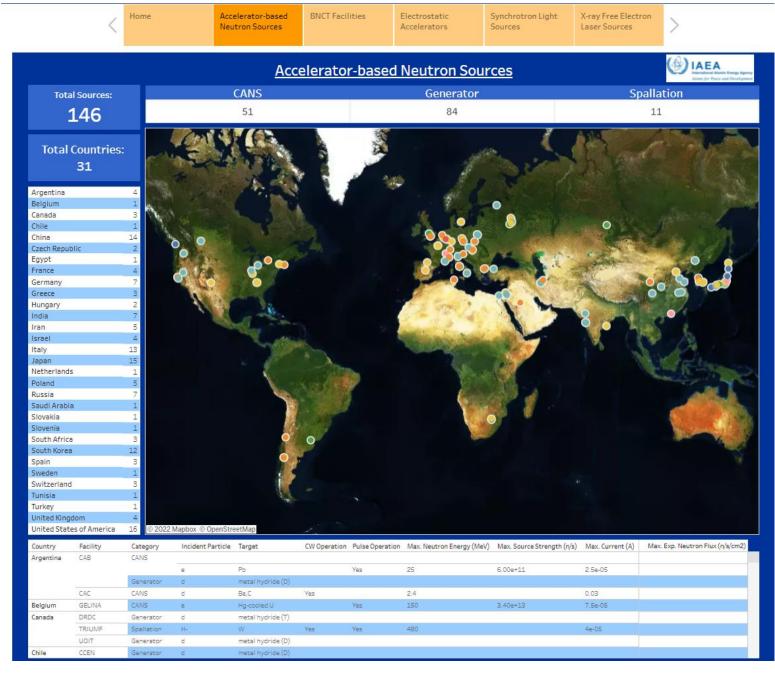


Allgemeines / General Band / Volume 7 ISBN 978-3-95806-280-1



## IAEA Databases

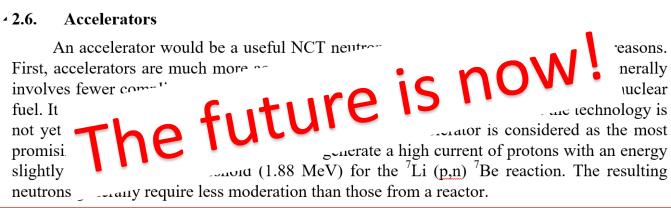
- Include CANS, BNCT, but also ion beam accelerators, synchrotrons
- Allied databases on food irradiators and fusion facilities, medical cyclotrons neutron scattering instruments.
- Please feed back any updates/corrections



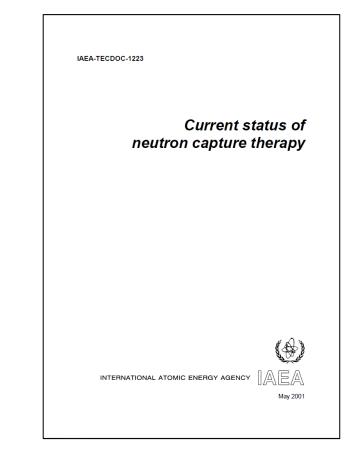
https://nucleus.iaea.org/sites/accelerators/Pages/default.aspx

# Boron Neutron Capture Therapy

- In 2001, IAEA published TECDOC-1223, "Current status of neutron capture therapy"
- RRs were the only neutron source strong enough for use.  $\Phi_{epi}$ >5×10<sup>8</sup> cm<sup>-2</sup>s<sup>-1</sup>



- Almost all the RRs involved in clinical trials for BNCT in 2001 are now closed.
- TECDOC-1223 remained a standard reference for the field but was in need of updating





			Beam	Current	Final	Refs.
			energy	goal	power	
Institute	Machine status	Target reaction	(MeV)	(mA)	(kW)	
	CYC	LOTRONS				
Kyoto University, Japan	Clinical trials and research	5.5 mm <sup>9</sup> Be( <u>p.n</u> )	30	1	30	[7, 29]
Southern Tohoku Hospital, Japan	Treatments covered by insurance	5.5 mm <sup>9</sup> Be( <u>p.n</u> )	30	1	30	[7, 29 54]
Kansai BNCT Research Center, Japan	Treatments covered by insurance	5.5 mm <sup>9</sup> Be(p,n)	30	1	30	[7, 29, 31]
	ELECTRODYNAM	IC LINEAR ACCELERA	TORS			
A-BNCT, DawonMedax, South Korea	RFQ-DTL: Preclinical	Thick <sup>9</sup> Be(p,n)	10	8	80	[55]
Fsukuba, Japan	RFQ-DTL: Preclinical	0.5 mm <sup>9</sup> Be( <u>p.n</u> )	8	10	80	[32, 71]
SARAF, <u>Soreq</u> , Israel <sup>*</sup>	RFQ-DTL: Under development	Liquid jet Li( <u>p,n</u> )	2.5	20	50	[34]
NFN, Legnaro, Italy <sup>*</sup>	RFQ: Under development	Solid <sup>9</sup> Be(p,n)	5	30	150	[56]
HEP, BNCT-01, Dongguan, China	RFQ: Operational	Solid <sup>7</sup> Li(p,n)	3.5	5	17.5	[57]
HEP, BNCT-02, Dongguan, China	RFQ: Operational	Solid <sup>7</sup> Li(p,n)	2.8	20	56	[57]
National Cancer Center, Tokyo	RFQ: Clinical trial	Solid <sup>7</sup> Li(p,n)	2.5	20	50	[33,37,38, 58]
Edogawa Hospital, Japan	RFQ: Commissioning	Solid <sup>7</sup> Li(p,n)	2.5	20	50	[7]
× • · · •	<b>x</b>	ATIC ACCELERATORS				
Budker Institute, Novosibirsk, Russia*	VITA: Operational	Solid <sup>7</sup> Li(p,n)	2.0-2.3	10	23	[46]
Blokhin Cancer Center, Moscow, Russia	VITA: Under construction	Solid <sup>7</sup> Li(p,n)	2.3	7	20	[59]
Kiamen Humanity Hospital, China	VITA: Commissioning	Solid <sup>7</sup> Li(p,n)	2.5	10	25	[46, 60, 61]
CNAO, Pavia, Italy	VITA: Under construction	Solid <sup>7</sup> Li(p,n)	2.5	10	25	[46]
Nagoya University, Japan	Dynamitron: Commissioning	Solid <sup>7</sup> Li(p,n)	2.8	15	42	[62, 63]
Birmingham University, UK*	Single ended: Under installation	Solid <sup>7</sup> Li(p,n)	2.6	30	78	[64, 65]
Helsinki University Hospital, Finland	Single ended: Commissioning	Solid <sup>7</sup> Li(p,n)	2.6	30	78	[66]
Shonan Kamakura Hospital, Japan	Single ended: Under installation	Solid <sup>7</sup> Li(p,n)	2.6	30	78	[67]
University of Granada, Spain	Single-ended: Under development	Solid <sup>7</sup> Li(p,n)	2.1	30	63	[68, 69]
CNEA, Buenos Aires, Argentina	ESQ: Under development	<sup>9</sup> Be(d,n) thin 8 μm <sup>13</sup> C(d,n) thick	1.45	30	43	[7, 8, 9]
KIRAMS	ESQ: Under development	${}^{9}\text{Be}(d,n)$ thin 8 $\mu$ m ${}^{13}\text{C}(d,n)$ thick	1.45	30	43	[7, 8, 9]

#### TABLE 5. CURRENT STATUS AND PERFORMANCE OF THE DIFFERENT ACCELERATORS INTENDED FOR AB-BNCT FACILITIES

Notes: \*Non-clinical facilities. The KIRAMS project is within a collaborative agreement with CNEA, Argentina.

30 MeV cyclotron at Kansai BNCT Medical Center

### BNCT: not a simple regulatory environment

- For clinical use, approval of the accelerator [medical device], a treatment planning system [software as a medical device], and a Bcontaining pharmaceutical [new drug submission] are required.
- In Japan, approval route was of all three was via "SAKIGAKE", similar to "Breakthrough therapy" [USA], ""Priority Medicines" [EU]

Accelerator + dose engine: Sumitomo Heavy Industries	Treatment planning system: RayStation	Pharmaceutical: Stella Pharma
ے۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔۔	RaySearch Laboratories >EN	Q MENU March 25, 2020 STELLA PHARMA March 25, 2020 STELLA PHARMA CORPORATION
for manufacturing and sales of accelerator based BNCT system and the dose calculation program in Japan World's first BNCT systems as medical device -	November 11, 2020 RAYSTATION SUPPORT FOR BORON NEUTRON CAPTURE THERAPY NOW IN CLINICAL USE IN JAPAN RaySearch Laboratories AB (publ) has announced that treatment planning system RayStation®' is now in clinical use with boron neutron capture therapy (BNCT) - along with treatment machine from Sumfarm Newy Industries, Ltd (SHI) - at two leading cancer clinics in Japan	STELLA PHARMA Receives Marketing and Manufacturing Approval in Japan for "Steboronine <sup>®</sup> Intravenous Drip Bag 9000mg/300mL" ~ World's First BNCT Drug ~

The first clinical application concerns treatment of unresectable recurrent head and neck tumors and is covered by Japanese national health insurance since June 1, 2020.

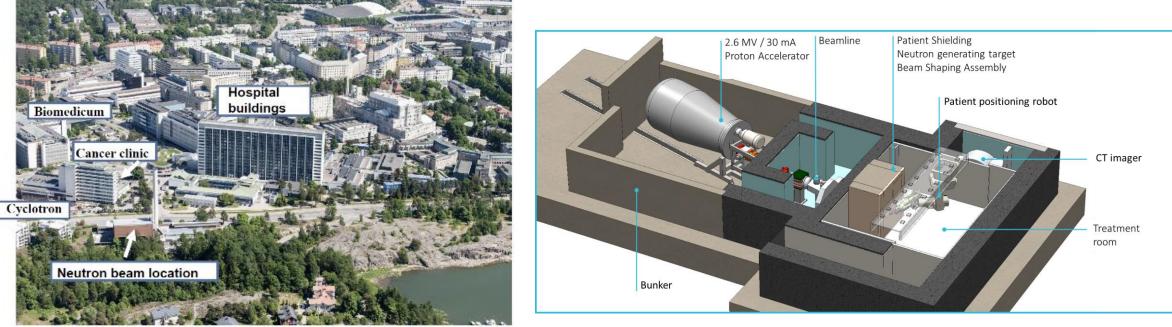
#### 30 MeV cyclotron at Kansai BNCT Medical Center





The first clinical application concerns treatment of unresectable recurrent head and neck tumors and is covered by Japanese national health insurance since June 1, 2020.

#### Accelerator based BNCT: status in Finland

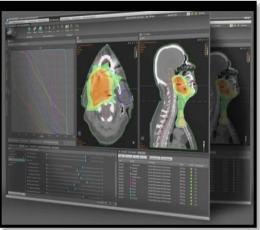


#### **Imaging Position**

#### **Treatment Position**





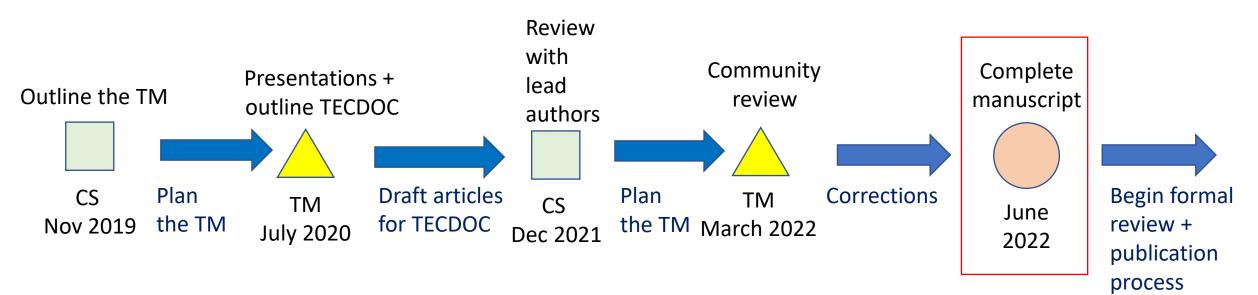






### Advances in Boron Neutron Capture Therapy

- The process leading to development of the TECDOC is outlined below
- As of today, we are fixing the last few small corrections before we begin the formal submission process.



#### CONTENTS

1	INTRODUCTION1			
	1.1	BACKGROUND	1	
	1.2	OBJECTIVE	3	
	1.3	SCOPE	3	
	1.4	STRUCTURE	3	
2	ACCE	LERATOR BASED NEUTRON SOURCES FOR BNCT TREATM	ENT	
-		LITIES		
	2.1	NEUTRON PRODUCTION	5	
	2.2	2.1.1 Neutron production reactions		
		2.1.2 Low energy proton reactions		
		2.1.3 Low energy deuteron reactions		
		2.1.4 Other neutron producing reactions		
	2.2	TARGET MATERIALS		
		2.2.1 Thermal loading of the target	14	
		2.2.2 Blistering and mechanical issues	14	
	2.3	ACCELERATORS		
		2.3.1 Electrostatic accelerators	15	
		2.3.2 Linear RF electrodynamic accelerators	16	
		2.3.3 Cyclotrons	16	
	2.4	COMBINATIONS OF ACCELERATORS AND REACTIONS	17	
3	DEAN	DESIGN CONSIDERATIONS	21	
2				
	3.1	ROLES AND REQUIREMENTS OF A BEAM SHAPING ASSE		
	3.2	BEAM SHAPING ASSEMBLY		
		3.2.1 High-energy neutron filter		
		3.2.2 Moderator		
		3.2.3 Neutron reflector		
		3.2.4 Thermal neutron filter		
		3.2.5 Gamma ray filter		
		3.2.6 Collimator		
		3.2.7 Beam aperture		
		3.2.8 Shielding		
	3.3	SUMMARY OF REFERENCE BEAM QUALITY FACTORS		
4	PHYS	ICAL DOSIMETRY AND DETERMINATION OF NEUTRON FIE	ELD	
	PARA	METERS		
	4.1	INTRODUCTION		
	4.2	RADIATION COMPONENTS IN BNCT		
	4.3	IN-AIR MEASUREMENTS		
		4.3.1 Neutron energy spectrum at the target		
		4.3.2 Neutron energy spectrum at the beam port		
		4.3.3 Neutron/gamma ray dose in the lateral direction		
		5 ,		

3

		4.3.4 Neutron spatial distribution	31
	4.4	IN-PHANTOM MEASUREMENTS	
	4.5	WHOLE BODY EXPOSURE	32
	4.6	REAL TIME BEAM MONITOR	32
		4.6.1 Electric current of the accelerated charged particle beam	32
		4.6.2 Real-time neutron monitor	
	4.7	MONITOR UNIT	33
	4.8	UNCERTAINTIES, TRACEABILITY	33
5	FACII	.ITY DESIGN	37
	5.1	PLANNING THE FACILITY	38
		5.1.1 Radiation safety	
		5.1.2 Classification of areas	
		5.1.3 Emergency response	
		5.1.4 Other considerations	
		5.1.5 Decommissioning of the facility	
	5.2	FACILITY RESOURCES	
	2.2	5.2.1 Neutron delivery and radiation protection	
		5.2.2 Patient care	
		5.2.3 Laboratory spaces	
		5.2.4 Option: Dedicated neutron analytical beamline	
		5.2.5 Option: Radiobiology laboratory	46
		5.2.6 Option: PET-CT system	46
6	OPER	ATION AND MANAGEMENT OF AN AB-BNCT FACILITY	
-	~ ~	THE DOLE OF FACILIDE OF SCIONAL AT A DATA CENTRE	47
	6.1 6.2	THE ROLE OF EACH PROFESSIONAL AT A BNCT CENTRE	
	6.2	PATIENT FLOW FOR A HEAD AND NECK CANCER PATIENT	
		CASE OF AN INDEPENDENT BNCT CENTER WITHOUT AN I PATIENT UNIT	
	6.3	CASE REVIEW CONFERENCE IN THE BNCT CENTRE.	
	0.2	INDIVIDUAL CLINICAL DEPARTMENTS AND THE CANCER	
		BOARD	-
	6.4	RADIATION EXPOSURE MANAGEMENT	
	6.5	MANAGEMENT OF A CLINICAL EMERGENCY.	
	6.6	SPECIAL CONSIDERATIONS FOR INTERNATIONAL PATIEN	
	0.0	SEEKING BNCT OVERSEAS	
		6.6.1 Prior to leaving for the destination country	
		6.6.2 In the destination country	
		6.6.3 After return to the departure country	
7	PHAR	MACEUTICALS AND RADIOPHARMACEUTICALS	
	7.1	REQUIREMENTS OF A BORON AGENT	55
	7.2	EARLY CLINICAL TRIALS OF BNCT	
	7.3	MERCAPTO-UNDECAHYDRO-CLOSO-DODECABORATE (BS	
	7.4	4-BORONO-L-PHENYLALANINE (BPA)	
		7.4.1 STRUCTURAL AND OPTICAL ISOMERS OF BPA	56
		7.4.2 DOSAGE FORM OF BPA	
		7.4.3 ADMINISTRATION METHOD OF BPA	57
	7.5	FUTURE PROSPECTS	58
	7.6	4-BORONO-2-[18F]FLUORO-L-PHENYLALANINE [18F-FBPA].	59

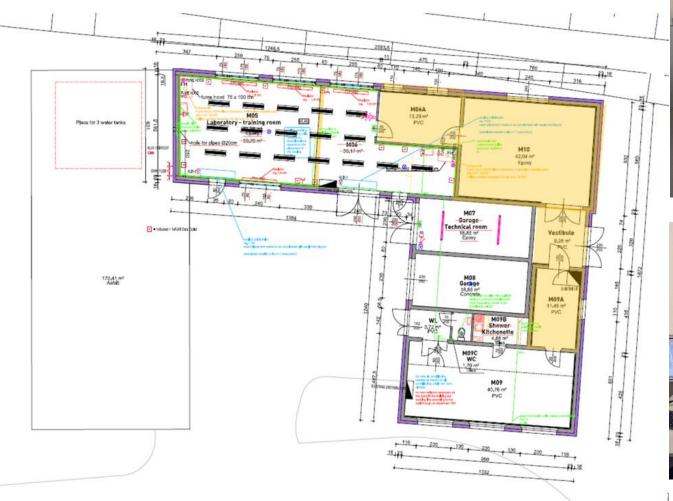
	7.7	USE OF <sup>18</sup> F-FBPA FOR POSITRON EMISSION TOMOGRAPHY (PET) IMAGING	50
		7.7.1 Synthesis	
		7.7.2 Tracer kinetics: uptake by tumours of <sup>18</sup> F-FBPA	
		7.7.3 Cellular transport mechanism of <sup>18</sup> F-FBPA/ <sup>18</sup> F-FBPA-fr	61
		7.7.4 Cellular metabolism of <sup>18</sup> F-FBPA	62
	7.8	<sup>18</sup> F-FBPA PET IN NORMAL HUMANS	
	7.9	DOSIMETRY OF <sup>18</sup> F-FBPA PET.	
	7.10	ANALYTICAL METHODS OF MEASURING <sup>18</sup> F-FBPA ACCUMULATION	
		7.10.1 Kinetic analysis	
		7.10.2 Single-time-point image analysis	
	7.11	CLINICAL APPLICATION OF <sup>18</sup> F-FBPA PET IMAGING	64
	/	7.11.1 Brain tumours	
		7.11.2 Head and neck tumours	
		7.11.3 Other tumours	
	7.12	OTHER APPLICATIONS OF <sup>18</sup> F-FBPA PET IMAGING	
	7.13	SUMMARY	
8	BORO	N CONCENTRATION DETERMINATION AND IMAGING	
	8.1	INTRODUCTION	
	8.2	TECHNIQUES USED IN BNCT CLINICAL PRACTICE IN AB-BN	
		8.2.1 Inductively Coupled Plasma (ICP) Atomic Emission Spectroscopy (ICP-AES) and ICP-Mass Spectroscopy (ICP-M	
		8.2.2 Ouantitative PET with <sup>18</sup> F-FBPA	
	8.3	8.2.2 Quantitative PET with <sup>18</sup> F-FBPA TECHNIQUES NOT CURRENTLY IN ROUTINE CLINICAL USE	
	8.3	AB-BNCT	75
		8.3.1 Prompt gamma analysis methods	
		8.3.2 Other prompt nuclear spectroscopic methods	
		<ul> <li>8.3.3 Neutron autoradiography with nuclear track detectors</li> <li>8.3.4 Quantification of boron distribution by Nuclear Magnetic</li> </ul>	
		Resonance (NMR)	
	8.4	8.3.5 Elemental imaging of boron in biological samples SUMMARY	
9	RADIO	DBIOLOGY	97
	9.1	THE BIOLOGICALLY EFFECTIVE DOSE OF BNCT	97
	9.2	PHOTON EQUIVALENT DOSE: CONCEPTS AND OUTLINE OF APPROACHES TO CALCULATION	
	9.3	RADIOBIOLOGICAL CONSIDERATIONS UNDERLYING AN IDEAL BORON CARRIER FOR BNCT	
	9.4	RADIOBIOLOGICAL CONSIDERATIONS UNDERLYING THE BORON CARRIERS EMPLOYED IN CLINICAL BNCT STUDIES (BPA, BSH, GB-10)	

40 (May 13)

9.5	MECHANISMS OF ACTION OF BNCT	103
9.6	APPLIED AND TRANSLATIONAL RESEARCH	106
	9.6.1 Optimization of tumour boron targeting	
	9.6.2 Strategies to improve BNCT efficacy and reduce radiotoxic	
	9.6.3 Research to identify the best candidates/treatment strategies	for
	BNCT	
	9.6.4 Biological studies reported for AB-BNCT	116
	9.6.5 Planning preclinical tests prior to clinical trials	116
	9.6.6 The activation of cells and animals	
	9.6.7 Determination of RBEs, CBEs, N/B (normal tissue/blood) a	
	T/B (tumour/blood) boron concentration ratios and other fac	
	0.4.0. The first increase is the section of the first increase in the first increase increase in the first increase in the first increase in the first increase increase in the first increase in the first increase increase in the first increase in the first increase in the first increase increase in the first increase increase increase in the first increase increase in the first increase inc	
	9.6.8 Radiation field size and effect on beam depth direction	
	9.6.9 Preclinical tests for new boron carrier drugs	
	9.6.10 Clinical biological studies	118
0.7	9.6.11 For future development of neutron capture therapy COMBINED THERAPIES	119
9.7 9.8	FUTURE PROSPECTS	
9.6	FUTURE FROSFECTS	121
METH	IODS AND MODELS OF DOSE CALCULATION	123
10.1	INTRODUCTION	123
10.2	GENERAL CONCEPTS	124
	10.2.1 KERMA and absorbed dose	124
	10.2.2 Nuclear and atomic data	125
	10.2.3 Macroscopic and microscopic scales	
10.3	METHODS FOR CALCULATING ABSORBED DOSES	
	10.3.1 Macroscopic calculation	130
	10.3.2 Microdosimetric calculations	135
10.4	MODELS FOR TRANSLATING BNCT DOSES INTO A REFER	
	RADIATION DOSE	138
	10.4.1 Motivation and general concepts	
	10.4.2 Reference radiation	139
	10.4.3 Relative Biological Effectiveness (RBE) and Compound	
	Biological Effectiveness (CBE)	
	10.4.4 The standard model based on single RBE and CBE values	
	10.4.5 Models for calculating photon isoeffective doses	
	10.4.6 Determination of radiobiological parameters	
	10.4.7 Range of validity and advice	149
PRES	CRIBING AND TREATMENT PLANNING	
11.1	INTRODUCTION	151
11.2	GENERAL ISSUES	
	11.2.1 Patient model	151
	11.2.2 Neutron 'beam' model	152
	11.2.3 Dose calculation.	152
	11.2.4 Quality assurance and calculation accuracy	153
	11.2.5 Monitor unit definition	154
11.3	AVAILABLE TREATMENT PLANNING SYSTEMS	155
11.4	PRESCRIBING BNCT	156

12	DOSE A	AND VOLUME SPECIFICATION FOR REPORTING IN BNCT1	59	
	12.1 12.2	THE NEEDS FOR HARMONIZATION OF DOSE REPORTING1 REPORTING CLINICAL DATA		
	12.2	ONCOLOGICAL CONCEPTS: GROSS TUMOUR AND CLINICAL		
	12.5	TARGET VOLUMES		
	12.4	SPATIAL CONCEPTS: PLANNING AND INTERNAL TARGET	60	
	10.5	VOLUMES	60	
	12.5			
	12.6	REPORTING DOSE IN BNCT		
		12.6.1 Dose components in BNC1 12.6.2 Reference point(s) and volumes for prescription and reporting.1		
		12.6.2 Reference point(s) and volumes for prescription and reporting. I 12.6.3 <sup>10</sup> B-concentration measurements and T/B and T/N ratios		
		12.6.4 Tissue element composition and RBE		
		12.6.4 Tissue element composition and RBE		
		12.6.6 Patient position and positioning error	62	
	12.7	ADDITIONAL POINTS TO BE NOTED IN BNCT		
13	CLINIC	AL TRIAL DESIGN AND PROCEDURES1	65	
	13.1	BACKGROUND OF MALIGNANT GLIOMAS INCLUDING		
		GLIOBLASTOMA	65	
	13.2	BACKGROUND OF HIGH-GRADE MENINGIOMA	65	
	13.3	BNCT FOR MALIGNANT GLIOMAS1	66	
		13.3.1 Newly diagnosed glioblastomas1		
		13.3.2 Recurrent glioblastomas		
	13.4	BNCT FOR HIGH-GRADE MENINGIOMA 1		
	13.5	FROM REACTOR TO ACCELERATOR	69	
	13.6	BACKGROUND OCCURRENCES OF HEAD AND NECK CANCEL		
		12 (1.0) 11 1		
		13.6.1 Squamous cell carcinoma		
		13.6.2 Non-squamous cell carcinoma	73	
	13.7	BNCT CLINICAL STUDIES FOR HEAD AND NECK CANCER 1		
	13.8	SKIN CANCER 1		
		13.8.1 Cutaneous malignant melanoma (CMm)		
		13.8.2 New directions in CMm treatment		
		13.8.3 BNCT for CMm	75	
		13.8.4 BNCT for other skin malignancies1	76	
	13.9	REGULATORY ASPECTS OF BNCT CLINICAL TRIALS	/6	
APPI	ENDIX I	FAST NEUTRON DOSE CONTRIBUTION1	79	
APPENDIX II. ICP METHODS IN USE AROUND THE WORLD				
REFERENCES				
ACCELERATOR-BASED BNCT PROJECTS AND FACILITY DESCRIPTIONS189				

### Neutron science facility at Seibersdorf











### Neutron Science Facility at Seibersdorf

- Consists of a pair of neutron generators: 1 D-D and 1 D-T
- DD operational. DT being commissioned shortly
- Development of teaching curriculum underway
- Intended for demonstration and training of neutron based techniques
- Neutron activation analysis
- Prompt gamma analysis
- Delayed neutron analysis
- Neutron imaging
- Production of tracers