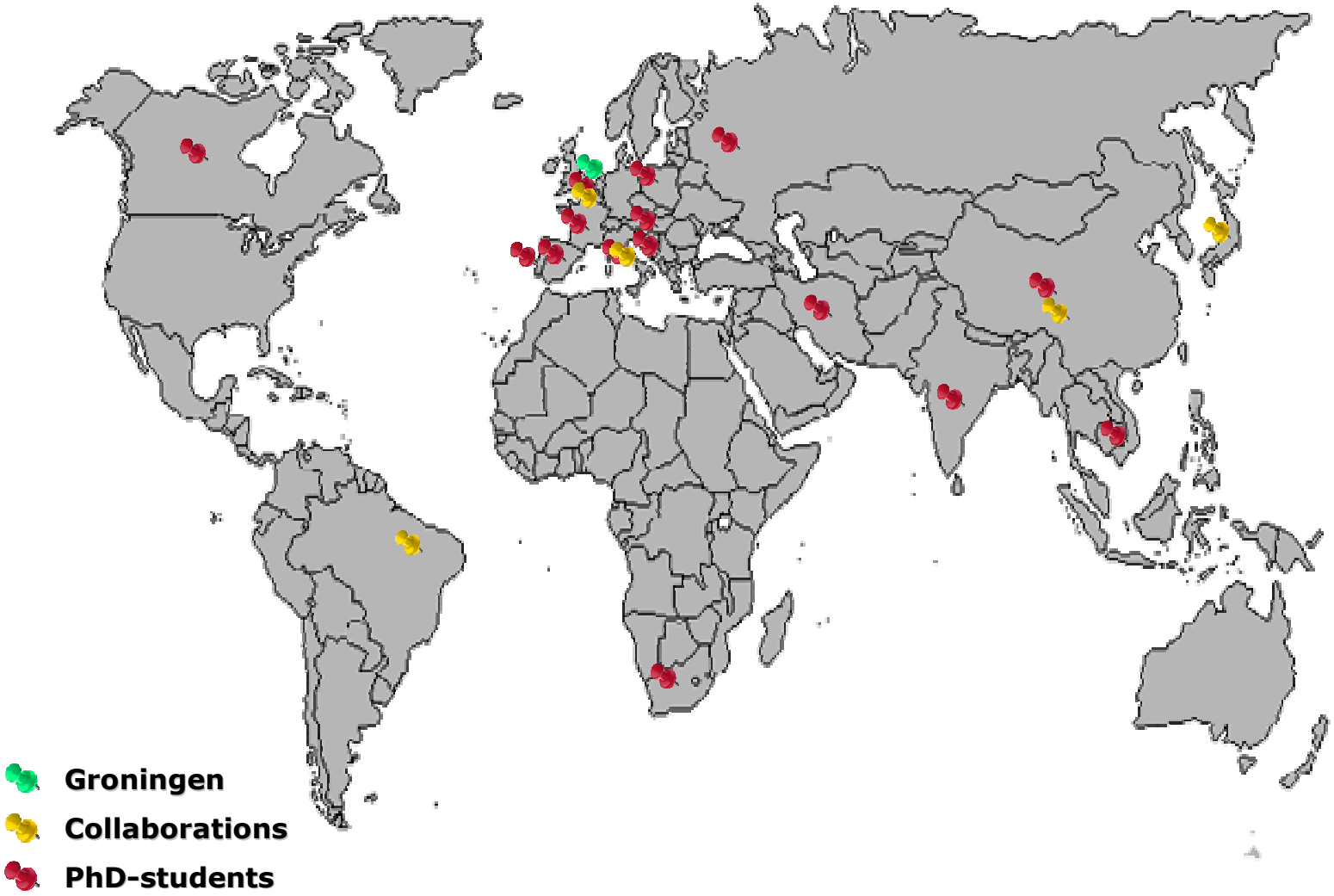
NUCLEAR MEDICINE & MOLECULAR IMAGING
UNIVERSITY MEDICAL CENTER GRONINGEN

- Is one of the largest hospitals in the Netherlands
- largest employer in the Northern Netherlands (>10.500)
- 1300 Beds
- 3500 Medical students

NUCLEAR MEDICINE & MOLECULAR IMAGING : AN INTERNATIONAL NETWORKSHAPER



INDUSTRIAL COLLABORATION

Contract research

- Bayer Schering Pharma
- Boehringer Ingelheim
- Daiichi Pharmaceutical
- Eli Lilly
- GlaxoSmithKline
- Johnson & Johnson
- MScience
- NeuroPharmaBoost
- PRA international
- QPS / Xendo

Academic collaboration with industries

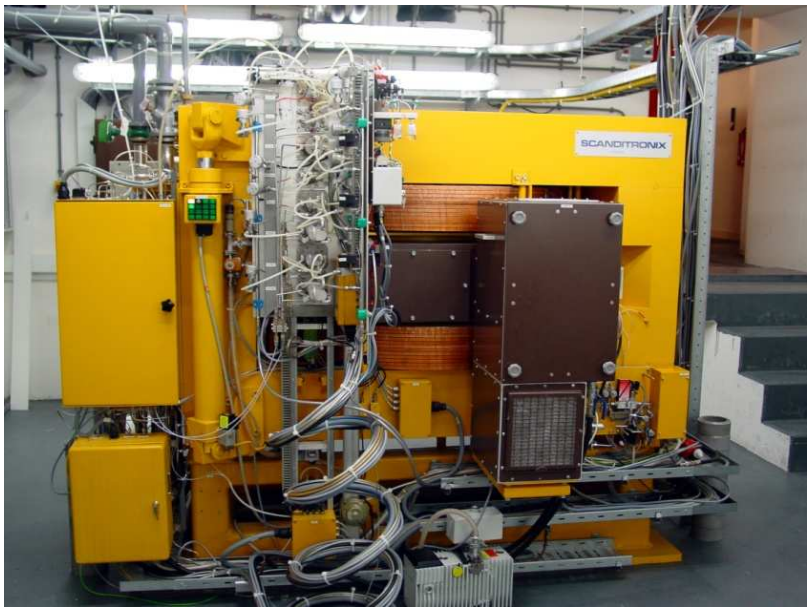
- Biomade
- Eckert & Ziegler
- QC1
- Raytest
- Roche
- TNO
- Siemens Medical
- Veenstra instruments

EQUIPMENT

- Siemens mCT (time-of-flight, HD, 64-slice CT)
- Siemens Ecat Exact HR+ PET camera

- Siemens Symbia T16 SPECT-CT (16-slice CT)
- Siemens Symbia T2 SPECT-CT (2-slice CT)
- 2 Siemens Symbia S1 gamma cameras
- Hologic Discovery Bone densitometer

The yellow monster



MC-17F GRONINGEN (installed in april 1991)

Two particle fixed-energy (17 MeV protons / 8.5 Mev deutrons)

Controlled by a PLC / STEP 5 Siemens

Targetladder: 8 targets (11C / 13N / 15O / 18F /18F2)

No beam line

"How we survived the last 20 years”

- Cyclotron production 2002-2010
- Annual unscheduled down time
- Stability & Acceptance test 2010
- Topics down time
- Down time 2003 & 2006
- Development
- Incident cyclotron door
- Topics of 2011
- The Answer

Jaap van Essen
Herman Keizer
Jitze Medema

Cyclotron production in 2002-2010

Total activity in GBq

radionuclide	2002	2003	2004	2005	2006	2007	2008	2009	2010
^{15}O	960	1700	3055	2090	920	336	239	885	**91**
^{13}N	1466	2300	2499	679	573	1234	1056	1110	**436**
^{11}C	22766	11900	9033	20519	27380	31317	33671	46349	**49687**
$^{18}F^{-}$	6701	5300	4044	5987	7683	9008	12868	13678	**15187**
$^{18}F_2$	599	800	926	2874	2837	2724	3784	2580	**2266**

11-C is number one

Cyclotron production in 2002-2010

Irradiations

radionuclide	2002	2003	2004	2005	2006	2007	2008	2009	2010
^{15}O	313	578	413	718	169	102	30	367	**20**
^{13}N	244	343	261	120	89	179	158	165	**71**
^{11}C	454	336	253	648	543	553	412	455	**437**
$^{18}F^-$	571	430	377	654	331	336	465	509	**562**
$^{18}F_2$	129	176	232	474	414	382	442	390	**348**

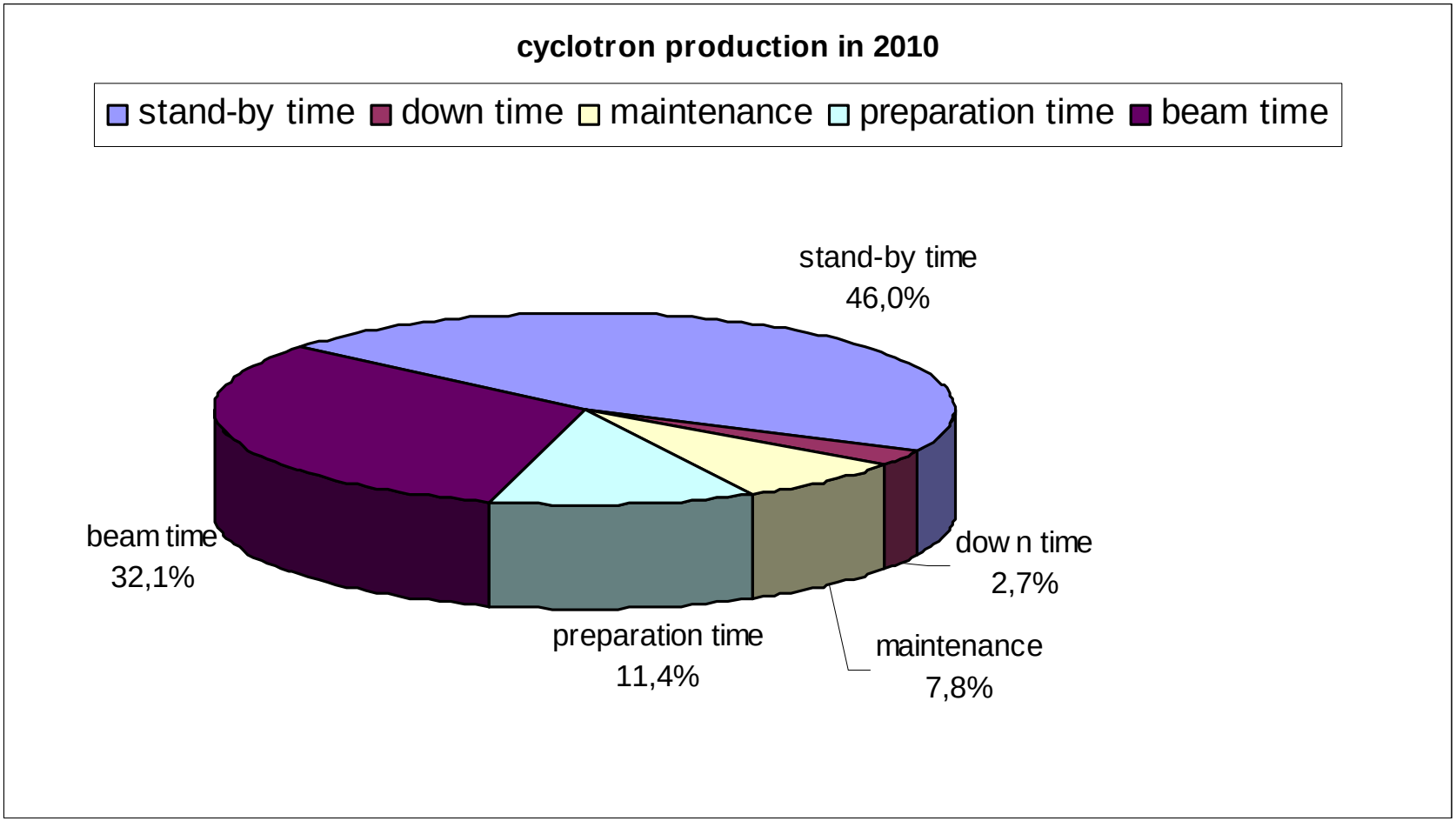
2010: Weekly about 30 irradiations

Results Protons / Deutrons last 8 years

		18-4-2011	16-4-2010	17-4-2009	29-2-2008	2-4-2007	24-5-2006	15-4-2005	12-3-2004
RESULTS PROTONS									
Beam internal	µA	5.5	8.6	7.6	8.5	7.0	10	10	10
Beam extern	µA	5.3	7.7	7.5	7.8	6.8	7.3	9	8.5
Beam FC	µA	5.2	7.2	7.4	7.6	6.6	6.8	8.8	7.8
FC1 right	µA	<	<	<	<	<	<	<	<
FC1 left	µA	0.1	0.2	0.1	0.1	0.1	0.3	0.1	0.1
ion source output	µA/ma	2.8	4.3	1.6	3.5	1	5	0.8	1.1
extr. Eff. (GOAL)	%	96	90	98	91	97	73	90	85
Transm. To FC	%	95	84	97	89	94	68	88	78
U-ARC	V	392	553	429	439	458	399	1278	68
RESULTS 50 µA on FC									
I-ARC	mA	29	20	54	36	17	26	59	47
U-ARC	V	1039	951	1640	1171	706	935	2136	1975
Gasflow	cc	1.7	1.9	2.5	3.0	3.6	3.7	6.0	3.0
ion source output on FC	µA/ma	1.7	2.5	0.9	1.3	2.9	1.9	0.8	1.1
RESULTS DEUTRONS									
Beam internal	µA	6.5	9.0	9.0	6.3	9.4	10	10	10
Beam extern	µA	4.7	6.1	6.8	4.8	6.1	5.9	6.5	6.3
Beam FC	µA	4.1	5.4	6.1	4.3	5.2	5.0	5.7	5.4
FC1 right	µA	0.05	<	0.2	<	<	<	<	<
FC1 left	µA	0.3	0.4	0.3	0.2	0.3	0.3	0.5	0.2
ion source output	µA/ma	3.3	2.3	3.0	3.2	3.1	2.5	1.7	5.2
extr. Eff. (GOAL)	%	72	68	76	76	65	59	65	63
Transm. To FC	%	63	60	68	68	55	50	57	54
U-ARC	V	405	557	579	456	456	509	911	687
RESULTS 60 µA on FC									
I-ARC	mA	17	26	17	24	15	23	>36	>46
U-ARC	V	985	1058	933	1027	790	1019	>2136	>2060
Gasflow	cc	3.0	3.1	3.0	3.0	3.5	3.3	6.0	3.7
ion source output on FC	µA/ma	3.5	2.3	3.5	2.5	4.0	2.2	0.8	1.1

High Extraction Efficiency for Protons (2010: 96%)

Production MC17 in 2010

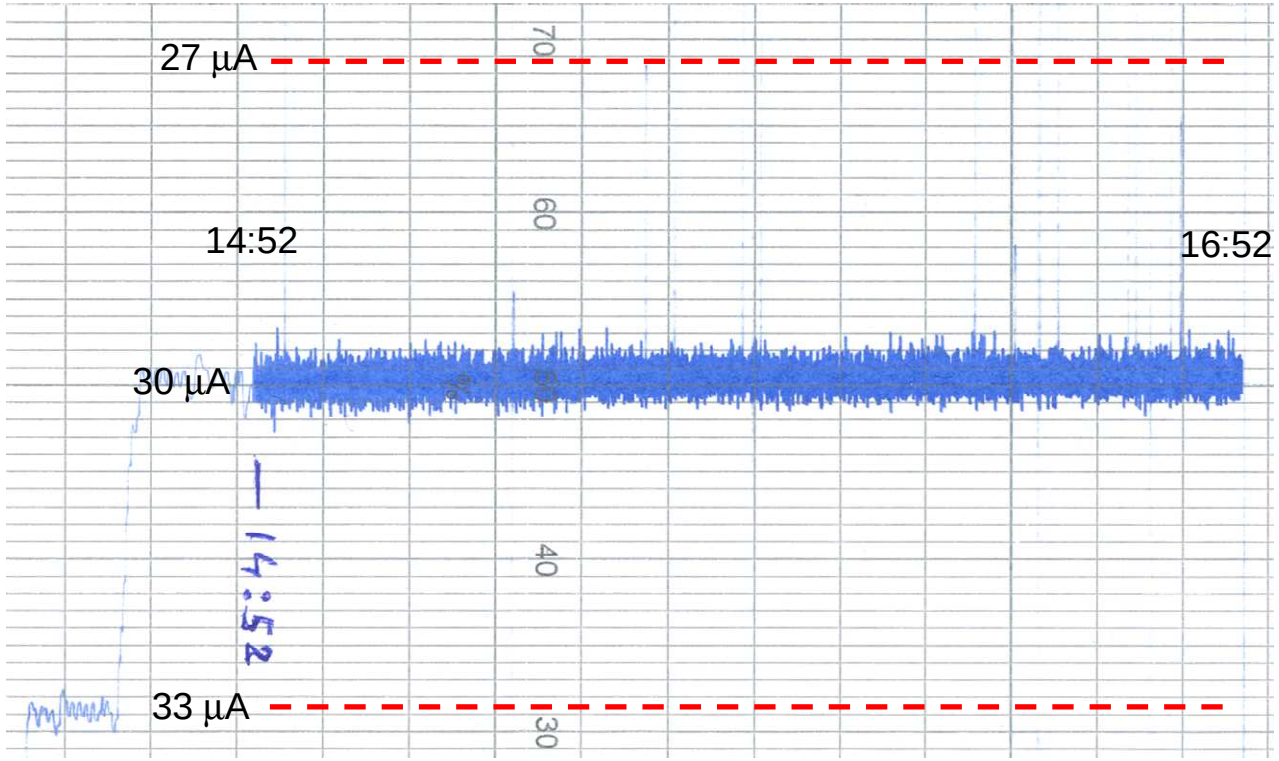


Overview of radiochemical synthesis for clinical use since 1992

	2010	2009	2008	2007	2006	2005	2004	2003	2002	2001	2000	1999	1998	1997	1996	1995	1994	1993	1992
^{18}F-FDG	280	264	256	262	225	272	251	239	219	222	200	210	191	147	101	95	105	110	82
^{18}F-Dopa	93	138	144	128	134	99	104	66	50	59	42	50	41	-	-	-	-	-	-
^{11}C-Methionine	42	52	56	48	38	29	22	16	6	-	-	-	-	-	-	-	-	-	-
^{11}C-HTP	42	55	38	37	60	7	-	-	-	-	-	-	-	-	-	-	-	-	
^{11}C-DASB	41	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
^{11}C-MDL	41	33	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$^{13}NH_3$	26	144	120	144	73	50	210	160	200	222	461	381	432	566	536	313	273	204	225
^{11}C-Choline	25	32	38	21	28	30	26	22	13	22	57	35	31	-	-	-	-	-	-
^{11}C-Raclopride	19	76	75	43	3	32	18	30	61	49	25	11	9	-	-	-	-	-	-
^{18}F-FLT	18	12	17	19	8	12	31	46	56	11	-	-	-	-	-	-	-	-	-
18F-FES	13	17	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
^{11}C-PK11195	12	5	23	38	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
^{11}C-SA4503	10	-	-	1	21	3	-	-	-	-	-	-	-	-	-	-	-	-	-
$H_2{}^{15}O$	9	362	20	30	126	538	393	507	245	491	557	448	216	234	724	581	629	290	154
^{11}C-MTO	6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
^{11}C-PIB	4	10	6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
^{11}C-Verapamil	3	-	44	4	30	40	-	2	24	14	15	10	-	2	-	-	-	-	-
^{18}F-FAZA	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
^{11}C-mHED	1	10	24	10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
^{18}F-DFMT	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
^{18}F-NaF	1	3	3	2	3	16	19	-	-	-	-	-	-	-	-	-	-	-	-
^{15}O-CO	-	-	-	-	-	4	-	-	-	-	1	5	4	4	11	17	-	-	-
^{18}F-FMISO	-	-	-	-	-	2	2	2	2	2	-	-	-	-	-	-	-	-	-
^{18}F-FHBG	-	-	-	-	4	1	-	-	-	-	-	-	-	-	-	-	-	-	-
^{11}C-CGP-12388	-	-	-	-	-	-	4	3	13	9	12	6	2	-	-	-	-	-	-
^{11}C-Carvedilol	-	-	-	-	-	-	1	2	-	-	-	-	-	-	-	-	-	-	-
^{11}C-Tyrosine	-	-	-	-	-	-	-	-	11	42	35	32	57	83	148	158	147	39	9
^{18}F-MPPF	-	-	-	-	-	-	-	-	9	9	8	10	2	-	-	-	-	-	-
^{11}C-Acetate	-	-	-	-	-	-	-	-	-	2	8	2	8	27	19	29	-	-	-
^{11}C-VC002	-	-	-	-	-	-	-	-	-	-	-	-	2	4	2	-	-	-	-
^{18}F-Fluorcarazolol	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5	14	3	-	-
^{11}C-Thymidine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	7	13	13	-
^{18}F-FESP	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	9	-	-
^{11}C-CGP-12177	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	16	6	-
^{11}C-Bicarbonate	-	-	-	-	-	-	-	-	11	34	12	-	-	-	-	-	-	-	-

Since 2000: 12 – 21 different radiochemical synthesis

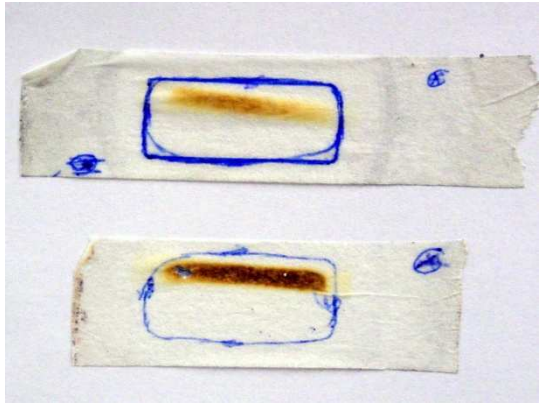
Stability test Protons 2010



Fluctuations fixed beamcurrent on FC during 2 hours

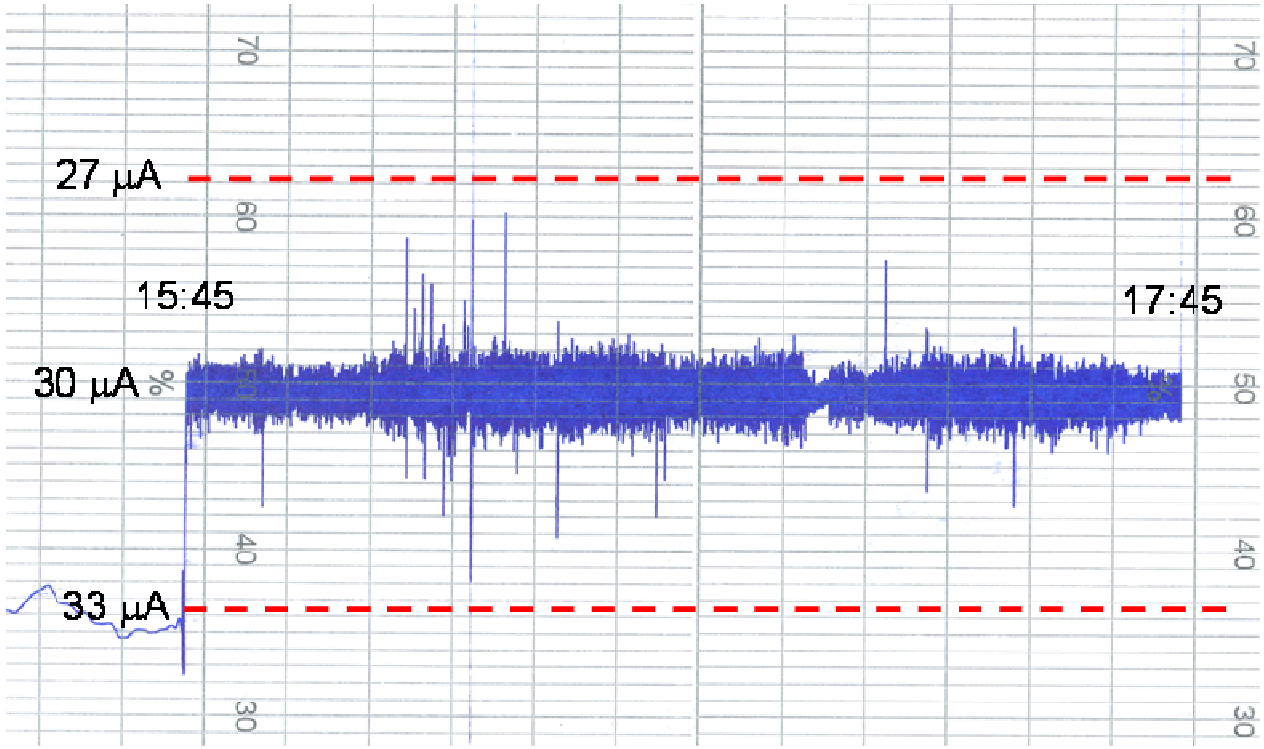
Acceptance test Protons 1991 vs 2010

	Acceptance test 22.03.1991	Re-acceptance test 01.09.2010
Beam current Faraday cup	**65 µA**	**65 µA**
Beam current External	**-**	**68 µA**
Beam current Internal	**74 µA**	**82 µA**
Current Ion source	**50 mA**	**28 mA**
Output of the ionsource:	**1,5**	**2,9**
Extraction coefficient.	**-**	**0,83**
Transmission to FC:	**0,88**	**0,79**



Typical beam profile protons

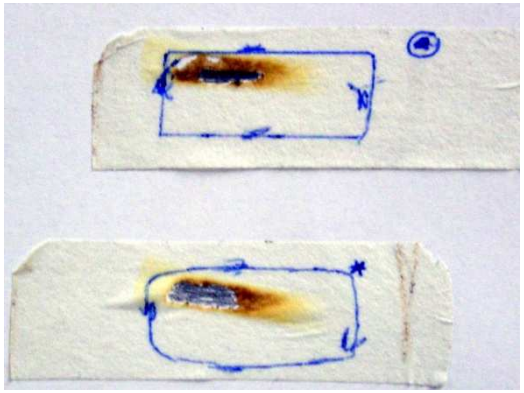
Stability test Deutrons 2010



Fluctuations fixed beamcurrent on FC during 2 hours

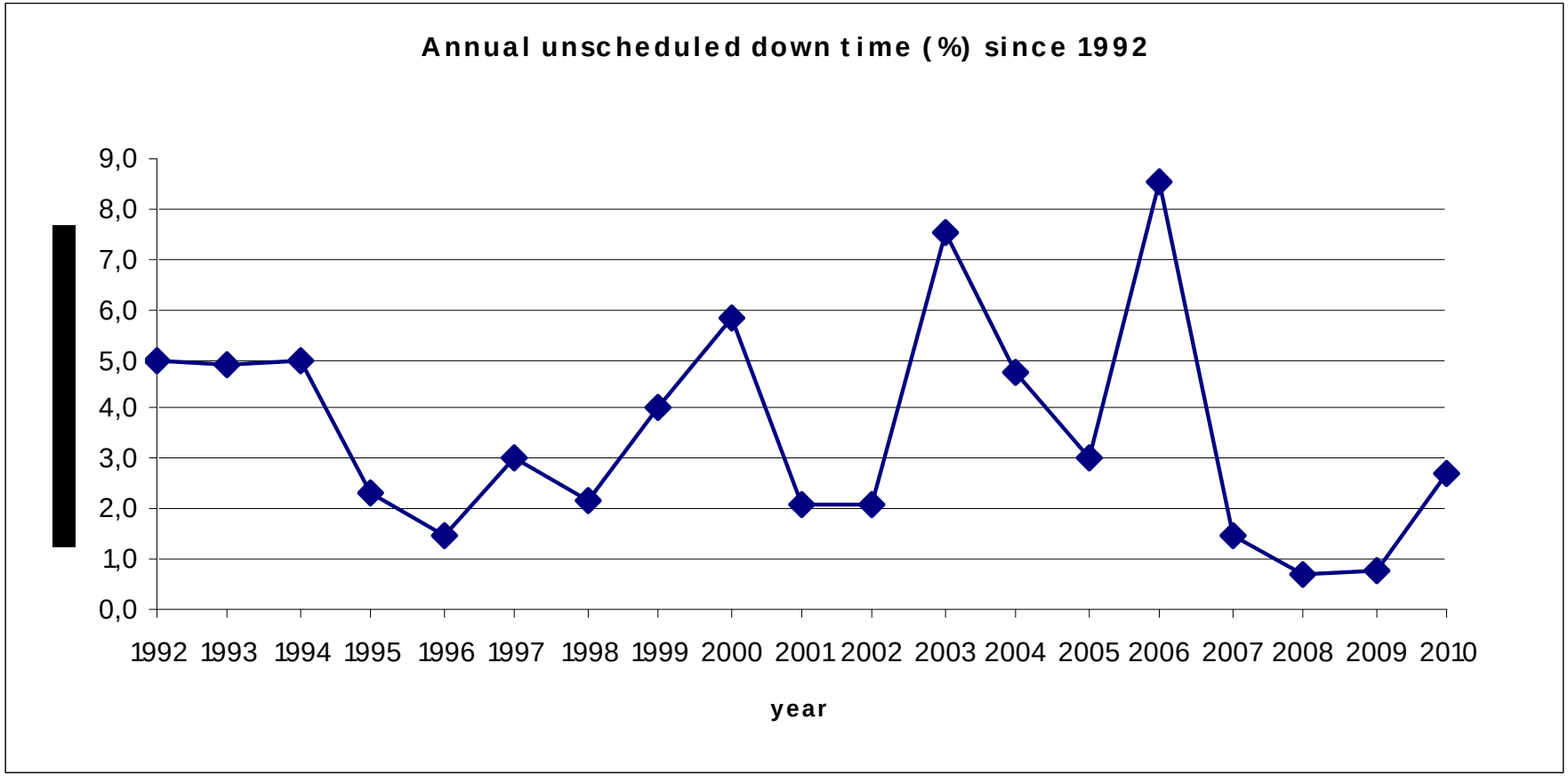
Acceptance test Deutrons 1991 vs 2010

	Acceptance test 22.03.1991	Re-acceptance test 01.09.2010
Beam current Faraday cup	**50 µA**	**50 µA**
Beam current External		**55 µA**
Beam current Internal	**78 µA**	**81 µA**
Current Ion source	**21 mA**	**18 mA**
Output of the ionsource:	**3,7**	**4,5**
Extraction coefficient.		**0,7**
Transmission to FC:	**0,6**	**0,6**



Typical beam profile deutrons

Annual unscheduled down time since 1992

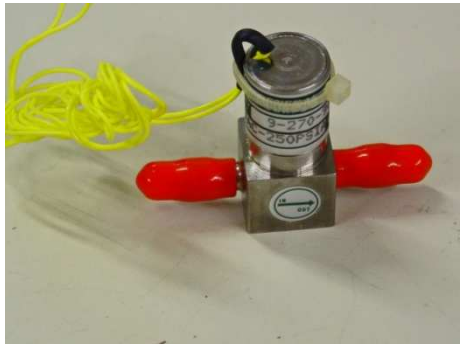


mean annual unscheduled down time: 3.6%

Topic down time: Valves

duty cycle 20%

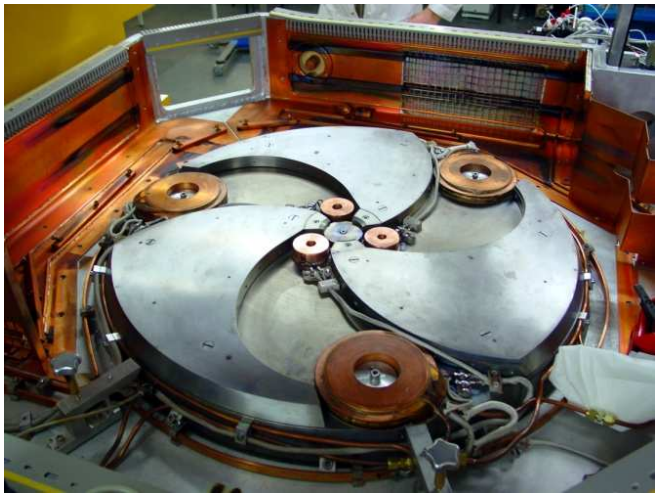
duty cycle 100%



1993: valve failure causes 4 hours down time every month

Topic down time: Gradient & Center Coils

- 1994: 3 gradient coils
  (total down time115 hours)
- 1999: C1
- 2001: 2 gradient coils
- 2004: A1
- 2005: A1
- 2006: A1, A2, A3 & 1 gradient coil

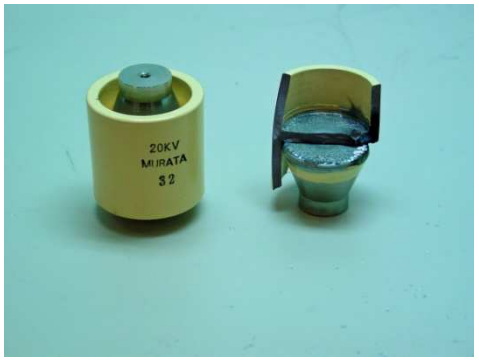


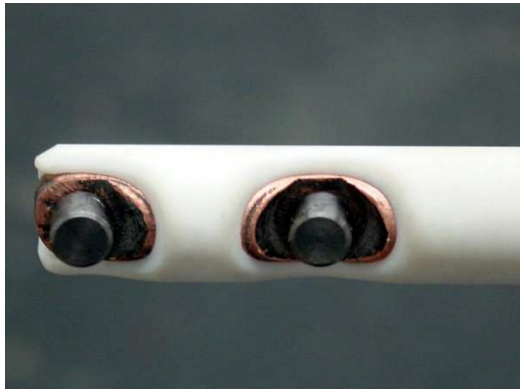
Burn connections of
the center coils

bad isolation

Other topics down time

- High humidity (dehumidifier in the vault)
- Target system failures (foils of the 18F2-target)
- Bellow FC (PM 3 times/year)
- PT for targets
- Deflector high current
- Capacitors PAMP
- Cathodes



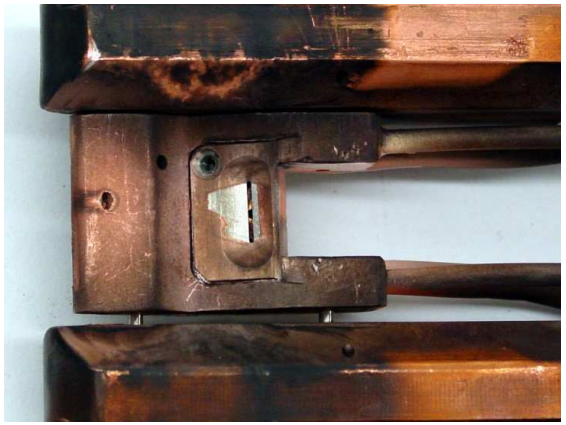


Radiation damage high pressure valve

VICI high pressure 2-position valve
for 18F targets

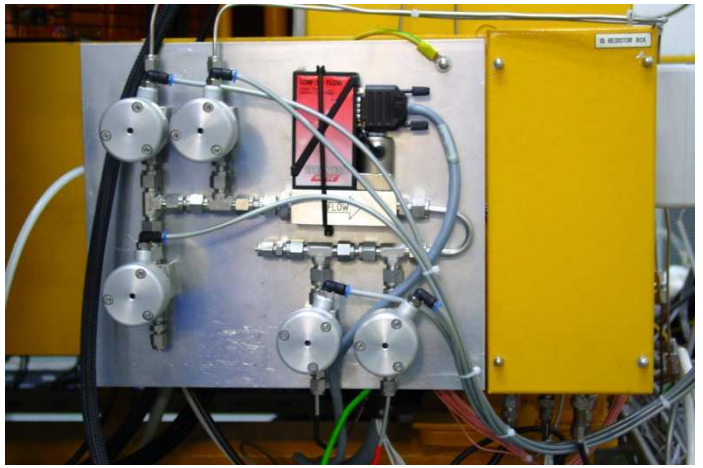
Down Time in 2003 (7.5%)

- Ion source problems (112 hours)
- RF problems (31 hours)



Hole in the ion source

Adjustment of the PAMP

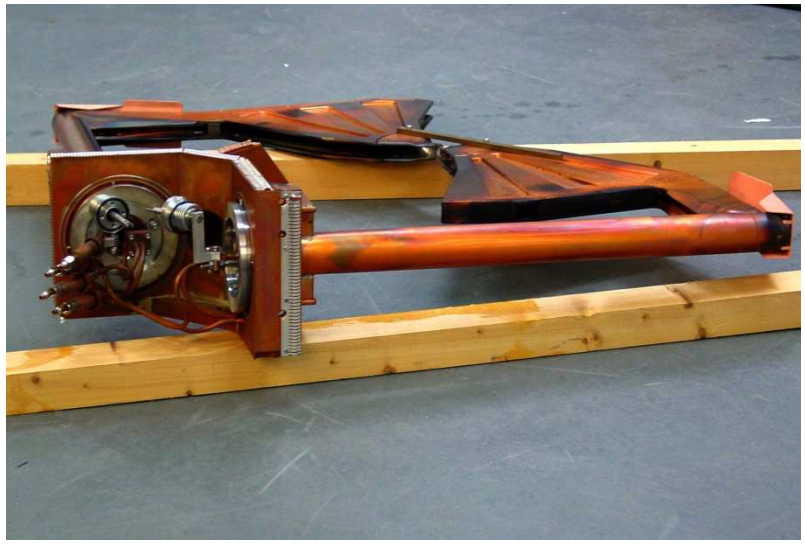


New valves ion source gasses

Down Time in 2006 (8.5%)

3 weeks down after 1 week PM

- Oil contamination of the copper parts of the vacuum chamber (151 hours)
- In 2010: Change of diffusion pump oil (santovac 5)



Cleaning of all copper parts

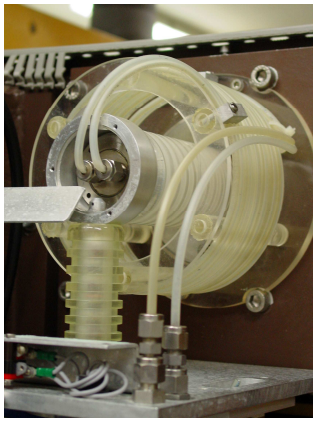
(Dee’s and Liners)

2008

- lowest down time in the history: 0.7% !!

Beer Time

An inside view of the cyclotron



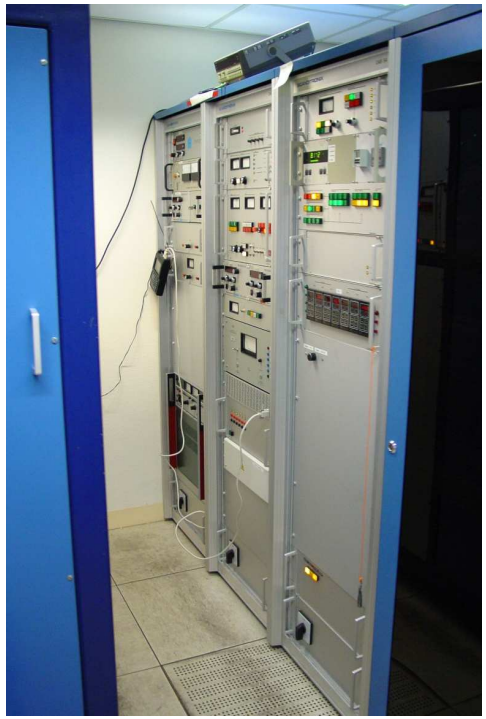
Deflector:

only 11 hours

(high voltage throughput system)

Development systems

The new pump for water cooling of the cyclotron

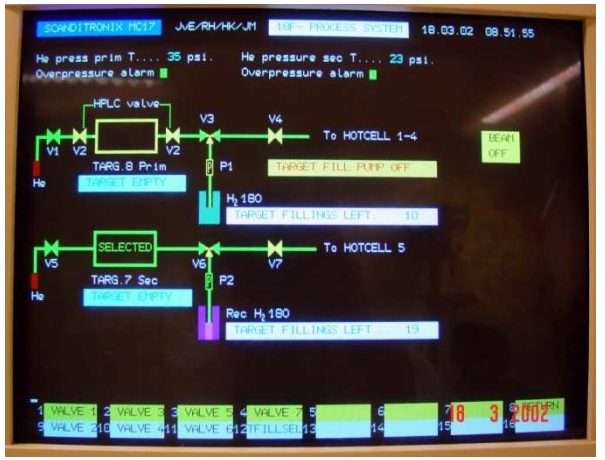


New Power Supplies:

- **Ion source**
- **Gradient coils**
- **RF power (RDRA)**

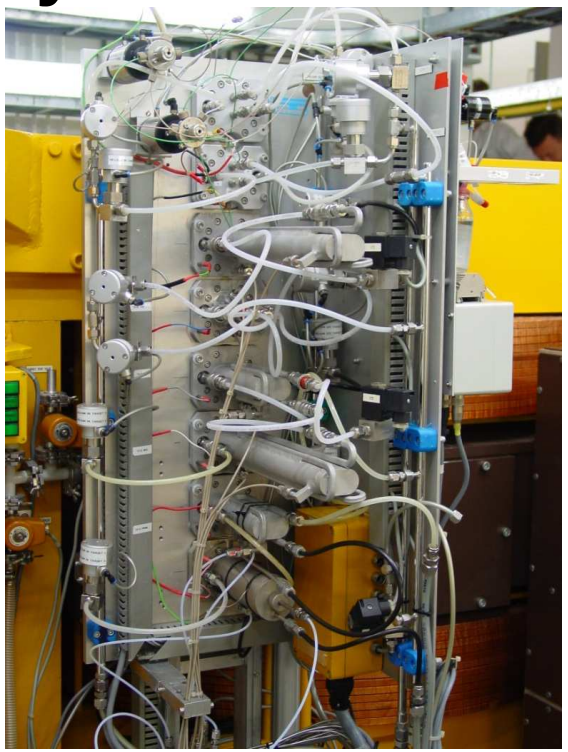
Development:
Programming in STEP 5

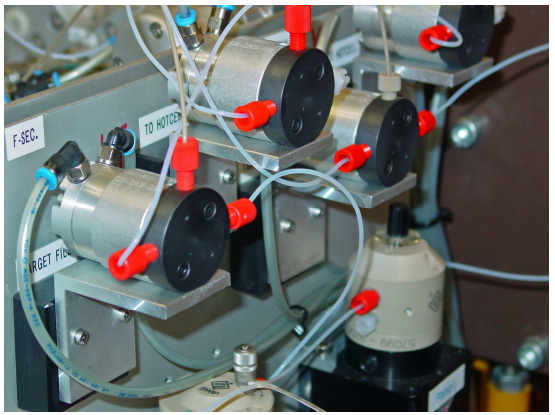
- Unattended start up cyclotron (18F and FDG-module)
- Filling system for 18F-Targets
- New pages: Vacuum & Watercooling status
- New process pages (11C /13N /15O /18F /18F2)
- Gas Delivery page integrated with the PET-scanner
- Automatically filling LN2 dewar in the vault
- Automatically Helium fill target cooling
- Ion source page (manual mode valves)
- Helium flush target cooling system (auto & manual mode)
- Leak test targets
- Activity Delivery System to new GMP-location



Development: Targetry

- All targets Helium & Water IN and OUT valve
- New PT's
- Automatically filling with 0.5% F2 carrier for the 18F2 target
- Target cooling 18F2 target
  (5 degrees Celsius)
- 15O target used for 18F2 production
- Change Teflon tubing to PEEK
- Helium cooling system: Copper ⇨ RVS
- New Helium cooling pump
- LEAK TEST gastargets
- New valves fluorine targets



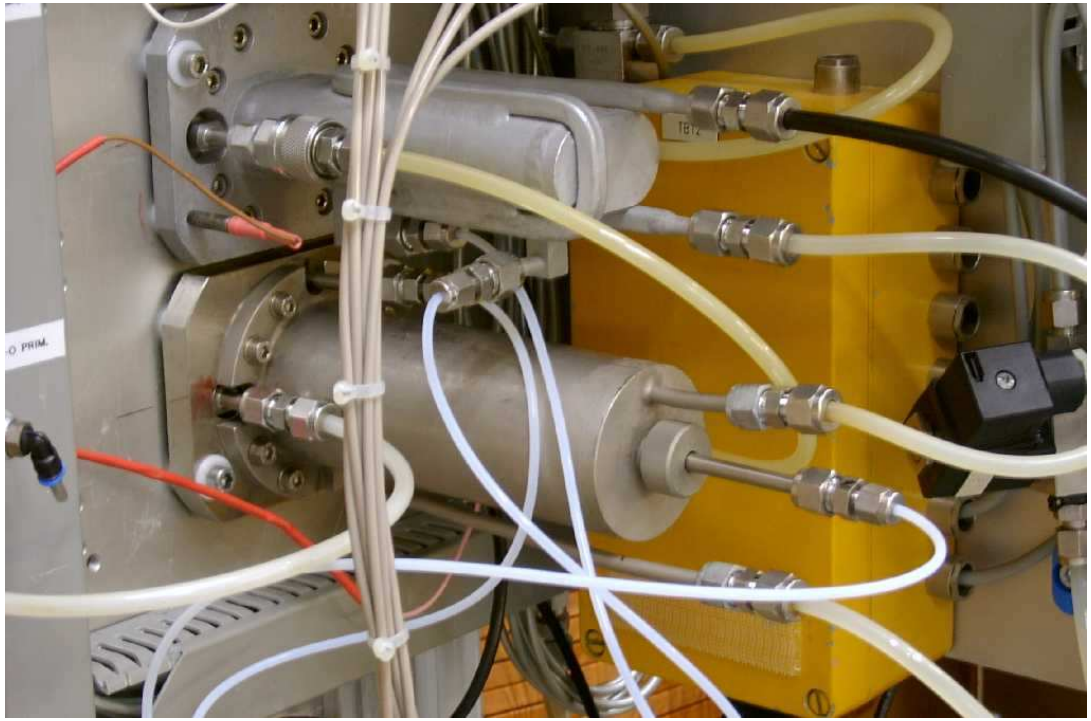


The new valves of the filling system for the fluorine targets

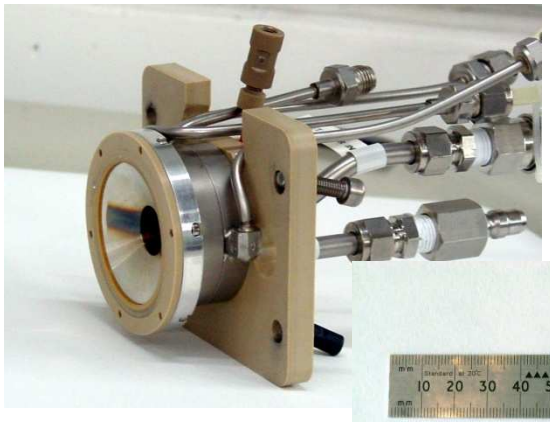
15O target used for 18F2 production

To improve the reliability of the production of FDOPA one of the 15O-targets (scanditronix) was used for the production of 18F-F2

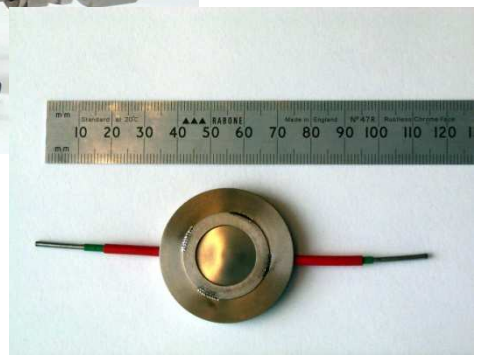
On the picture both targets are shown. The lowest target is the original 18F2-target. The upper target is the 15-O target made of Aluminium.

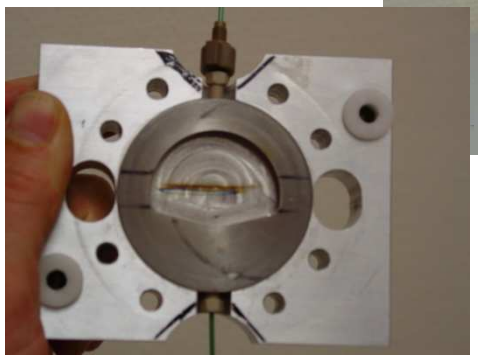


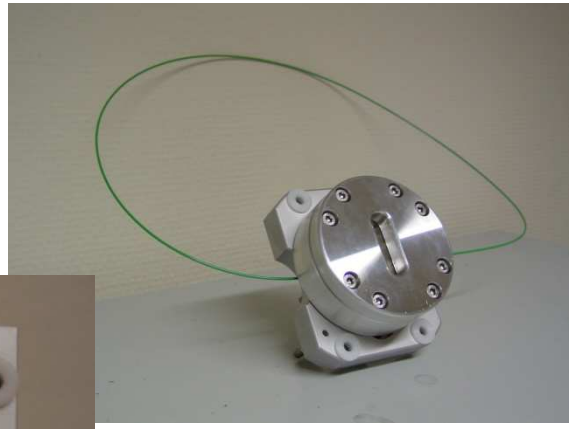
Development: 18-F Targets



Nuclear Interface







“LUND-target”

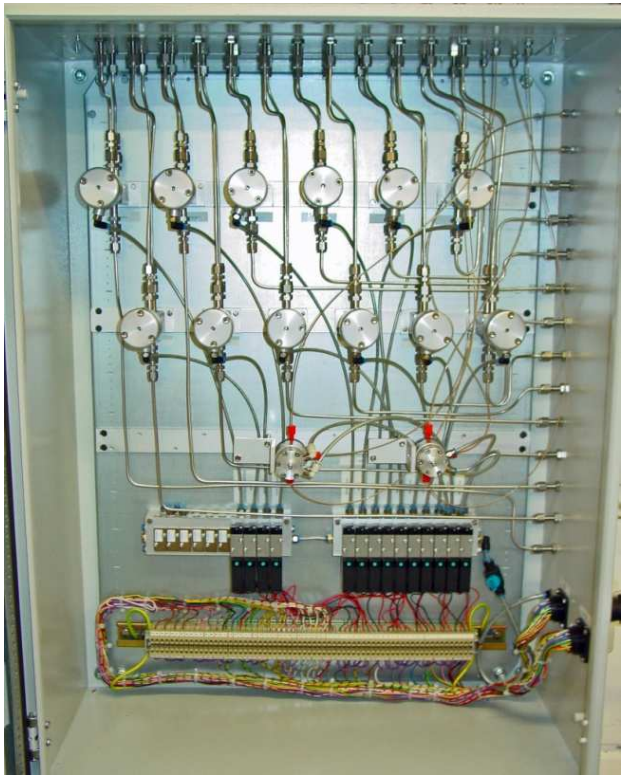
- **1991: SCX-targets** **Al/Ag 0.8 ml 15 uAh 13 GBq**
- **2001: Nuclear Interface target** **Titanium 1.0 ml 20 uAh 70 GBq**
- **2006: “LUND” design** **Niobium 3.0 ml 35 uAh >120 GBq**
  (cooperation: Groningen/Lund/Uppsala)

2010: Incident cyclotron door

Safety button opens the door automatically

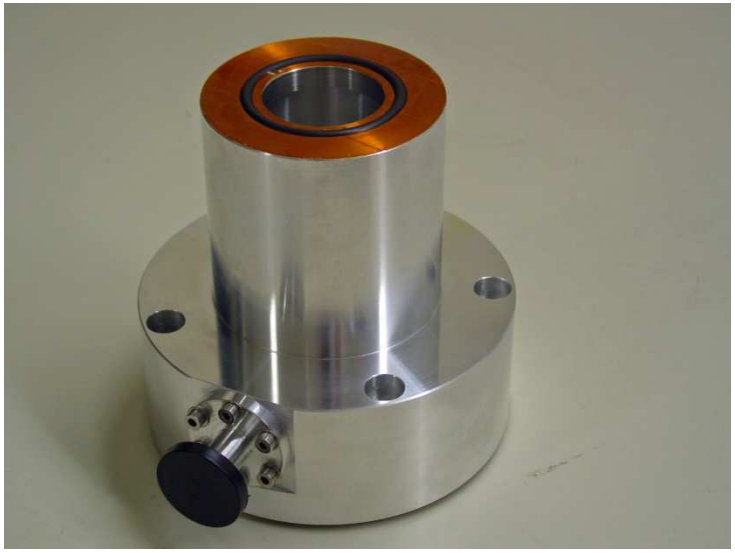
- Damage wall
- Almost broke the gas lines (1% F2, H2)

Topics last PM 2011



Delivery system in the vault for radionuclides to GMP-location (14 lines)

Frequently replacement of the O-ring of the target-chamber



New Target sluice

Decreased target coupling time from 90 sec to 20 sec

Topic of 2011

Herman 60 Year

Comparison
1992 vs 2010

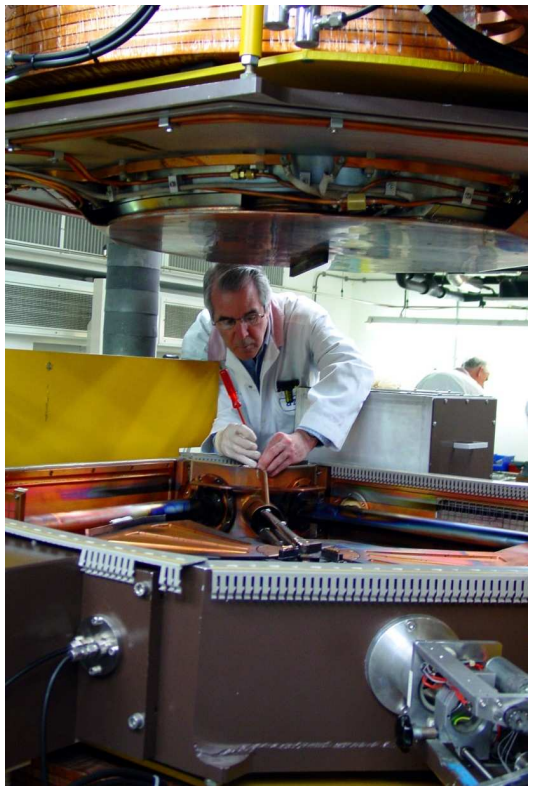
Item	1992	2010
Maintenance time	15%	7.8%
Beamtime	18%	32%
Radiofarmaceuticals	3	21

Status 2011:

- The machine is in control
- High level of knowledge hardware & software MC17
- Self supporting maintenance

Answer: "How we survived the last 20 years“

- Education for programming in STEP 5
- Interaction of the accelerators group and the chemistry (high service level)
- Availability of accelerators group (7:30 – 17:00)
- Scheduled maintenance time and time for development
  - ❖ Every Monday morning 2 hours
  - ❖ Yearly 7 mondays
  - ❖ PM (1 week)
- Cyclotron routine operating by the laboraty technicans
- Stock of critical spare parts (valves, bellows, coils, ...)
- Connections SCX Users group / IBA



Future

MC-17

Support:

- GMP productions
- Small Animal Facility
- R&D laboratory
- 89-Zr & 124-I production

IBA 18/18

Duaal beam

8 targets