CSN5 INFN new research project proposal
(2015-2017)

TECHN-Osp

R&D activities aimed at an industrially-based technology for future homeland accelerator-^{99m}Tc production based on a selected cyclotrons' network in Italy:

May the the colllaboration network gathered around the APOTEMA research project have a role as the strategic center for the scientific/technical support?

The APOTEMA/ S. Orsola (Bo) Hospital collaboration network for the next TECHN-Osp project

LNL, June 19th , 2014

APOTEMA

Accelerator-driven **P**roduction **O**f **TE**chnetium/**M**olybdenum for medical **A**pplications

Assessment of accelerator-driven alternative production of ^{99m}Tc (^{99}Mo) exploting the future, high current output, SPES proton cycloton at LNL in the framework of LARAMED project. ^{99m}Tc is currently the largest radionuclide used for diagnostic investigations in nuclear medicine deparments.

Tc-99m production →

- ^{100}**Mo**(p,2n)^{99m}**Tc** (direct route)
- ^{100}**Mo**(p,x)^{99}**Mo** → ^{99}Mo/^{99m}Tc generator

INFN Istituto Nazionale di Fisica Nucleare Laboratori Nazionali di Legnaro

The daily need of ^{99m}Tc in Italy

Some facts and starting numbers....

- Based on a first meeting occurred with the medical physics head of the St. Orsola Hospital (Bologna)-Nuclear Medicine Dept., we have been aware that:

- ^{99m}Tc needs for S. Orsola Hospital only for routine diagnostic procedures : 1÷2 Ci/day

- Required ^{99m}Tc daily activity needed for the whole country estimated to be about S. Orsola Hospital x 150 ≅ **150-300 Ci**
- Is this range likely?

- Former information we had for **Veneto region** in past years: ~10 Ci/day
  Rough extrapolation: 10x 20 Italian regions =200 Ci

- Former information we had for **Ferrara Hospital** in past years: ~1 Ci/day
  Emilia Romagna region estimated ~ 15 times Ferrara needs = 15 Ci/day x 20 = 300 Ci/day

The average ^{99m}Tc daily need may thus be supposed ~200 Ci in the whole country

INFN Istituto Nazionale di Fisica Nucleare Laboratori Nazionali di Legnaro

^{99m}Tc production expected using next high-performance cyclotrons

^{99m}Tc in-target production yields estimated at EOB after:

- 3 h irradiation,
- at 15 and 20 MeV,
- 200 μA beam current
- 500 W/cm^2 mean areal power density
- 99.05% ^{100}Mo enrichment (optimized target configuration).

A series of quality parameters are listed at EOB. (Ref. 2 RCM report, IAEA 2013)

^{99m}Tc production		Ep=15 MeV	Ep=20 MeV
Beam power on target	[kW]	3.0	4.0
Integral-target activity	[Ci]	2.85	5.56
In-target activity	[mCi/μA]	14.25	27.8
Specific Activity	[GBq/g]	$3.84 \cdot 10^7$	$2.96 \cdot 10^7$
Tc / TOTAL activity		0.9848	0.9468
^{99m}Tc / TOTAL activity		0.3693	0.3926
^{99m}Tc / $^{99m+g}$Tc		0.1990	0.1665
Isotopic Purity (IP)		0.1970	0.1520
Radionuclidic Purity(RNP)		0.3750	0.4147

→ **reference for 100 μA current**

1.4 and 2.8 Ci expect to be yielded, removing **1.5 and 2.0 kW power** respectively

Basically, the daily production needed by a Hospital !!!

INFN Istituto Nazionale di Fisica Nucleare
Laboratori Nazionali di Legnaro

The key issue of ^{100}Mo-enriched moly recovery...

The ^{100}Mo-enriched (>99%) metallic moly cost in huge amonts (i.e. several hundreads grams) is currently around **800 Euro/gram. Enriched-Mo recovery ia a mandatory step program.**

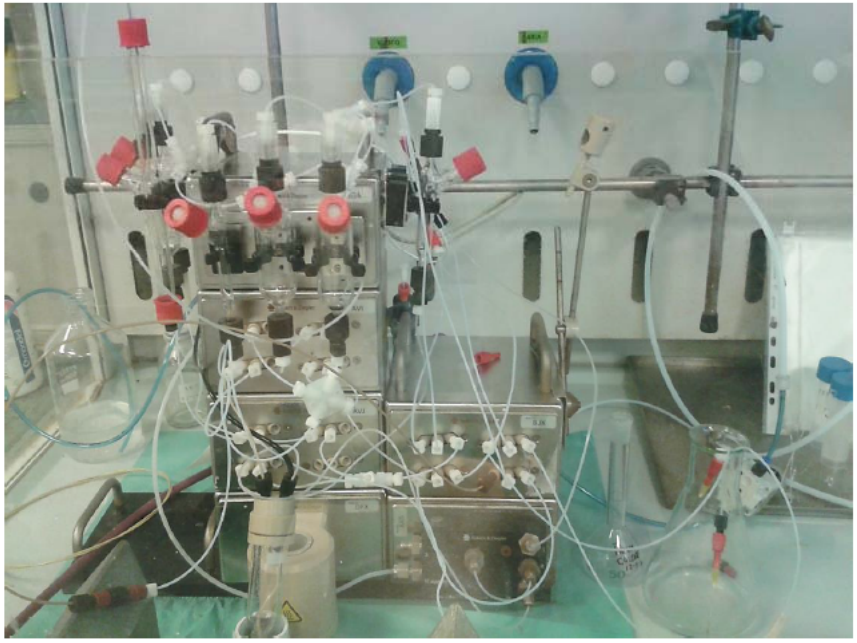
As comparison, cost for a few grams is ~1300 Euro/g

Coin target type	
Target diameter (coin type)	Φ = ~ 10 mm
^{100}Mo-enriched layer thickness required (i.e. optimized production for 18-20 MeV cyclotrons)	400 μm
Moly volume estimated	~ 31 mm^3
^{100}Mo-enriched moly metal bulk density	10.7 g/cc
moly mass estimated for any single target	336 mg

INFN Istituto Nazionale di Fisica Nucleare
Laboratori Nazionali di Legnaro

Automatic ^{99m}Tc separation Module optimization

First successful Tc99m separation test at high yield with an automated, remote-controlled system



- **~140 mg moly mass** treated
- n.6 laminated **^{100}Mo-enriched (99.05%) foils**
- **143 μm total thickness**
- Irraddiation test at the MC40 Cyclotron at JRC ISPRA done on **June 26, 2014. E=19 MeV 20μA**
- **~3.7 GBq (100 mCi)** Tc99m in-target yield.
- Radiochemical dissolution-separation test done at Ferra , with the effective support of people from S. Orsola Hospital (Bologna)
- **~ 1.5 GBq (50 mCi)** Tc99m separated in pertechnetate form $TcO4^-$
- Gamma spectrometry showed the presence of only isotopes of Tc in the final product, with a **recovery yield of Tc-99m greater than 92% in 1 hour**.
- Data taking still ongoing (**gamma spectrometry measurements at LNL by at LARIM group**) to determine the radionuclidic quality of acceleraotor-Tc

Great collaboration from Medical Physics unit of S.Orsola Hospital (Bo)!!!

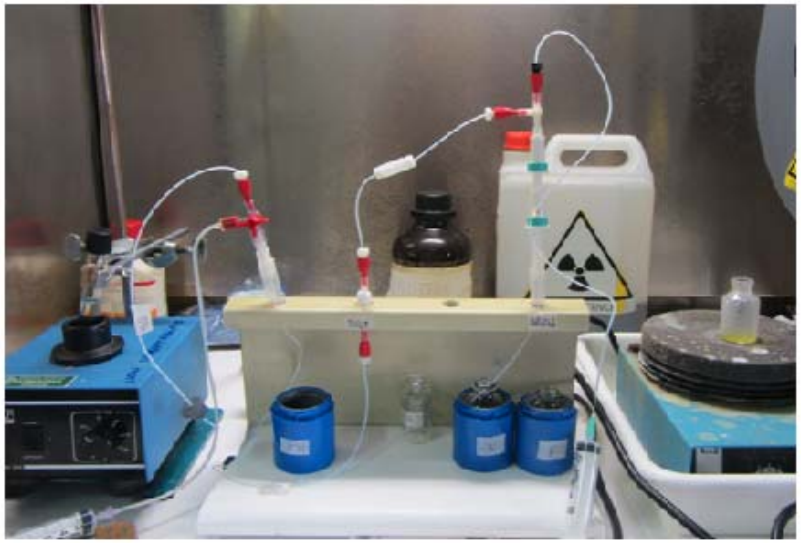
TEST PROTOTIPO MODULO PAVIA & FERRARA

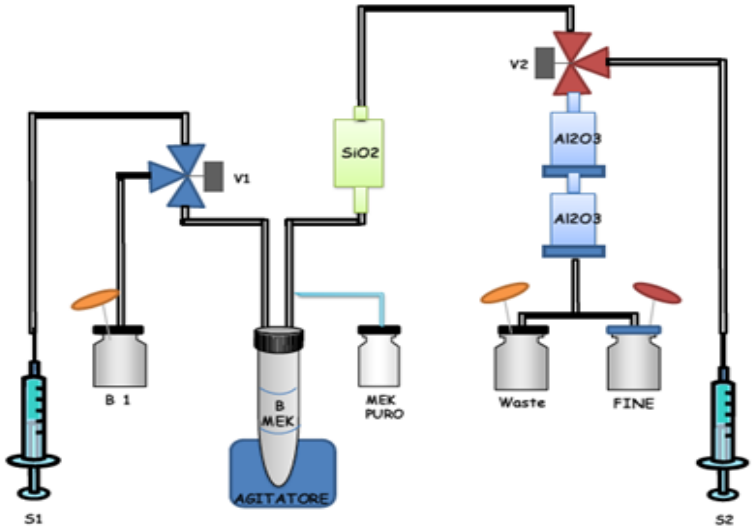
SCIOGLIMENTO TARGET: H_2O_2 a caldo + NaOH

$$Mo + 3\,H_2O_2 \rightarrow MoO_3 + 3H_2O$$

$$MoO_3 + 2NaOH \rightarrow Na_2MoO_4 + H_2O$$

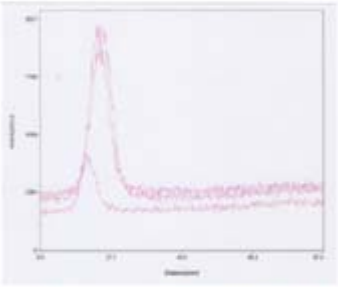
ESTRAZIONE:

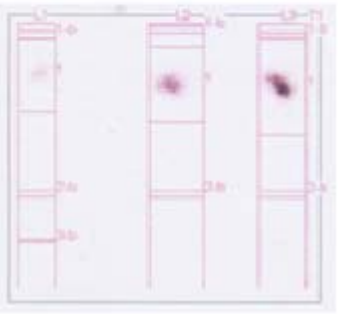




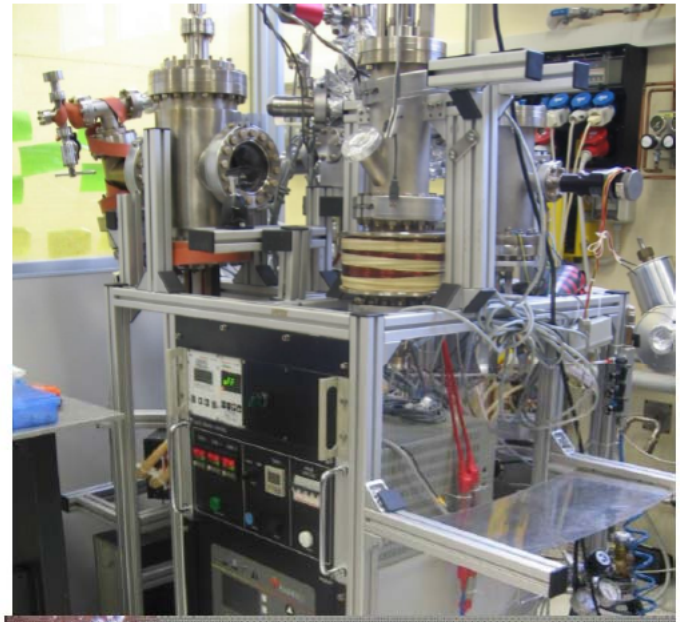
CONTROLLI QUALITÀ

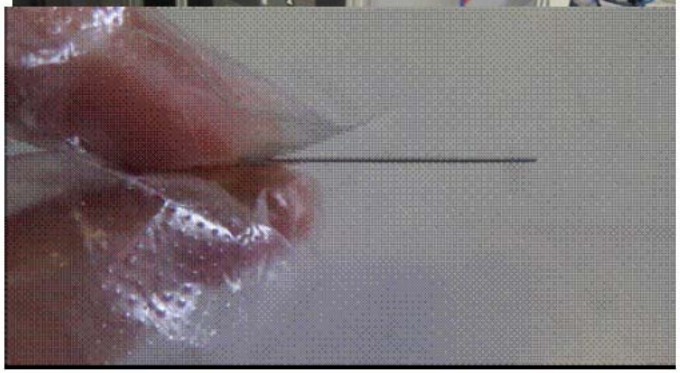
Purezza radionuclidica		**Mo-A**	**Mo-B**	**Mo-C**
	A_{Mo-99}/ A_{Tc-99m}	< MAR	< MAR	< MAR
	A_{Nb-97}/ A_{Tc-99m}	< MAR	< MAR	< MAR
	A_{Tc-93g}/ A_{Tc-99m}	0.15 %	0.11 %	0.11 %
	A_{Tc-94g}/ A_{Tc-99m}	0.23 %	0.20 %	0.17 %
Purezza chimica	**Mo-A-B-C**			
	pH		4,5-5	
	Mo		<5ppm	
	Al		<5ppm	
	MEK		<0.009% (v/v)	
Purezza radiochimica	100%			

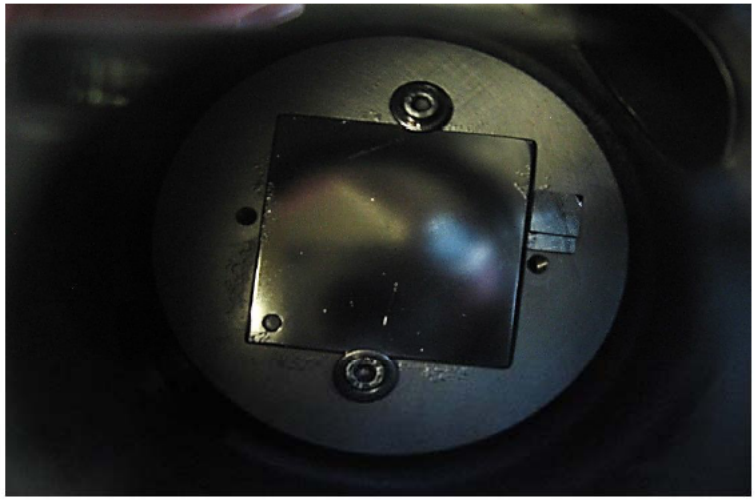




First tests and results at STS lab at LNL on molybdenum layer deposition on backing material







First successful test **to deposit multiple layers (0.5 μm each) up to ~300 μm on a copper backing** using the Physical Vapour Deposition (PVD) technique under UHV.

No stress at micro-structure level has been observed.

The system has been fully automated

Further tests are underway to **fully optimize the production process able to produce good quality layers** …

INFN Istituto Nazionale di Fisica Nucleare
Laboratori Nazionali di Legnaro

The new research plan proposed....

- The is a growing interest all over the world in the new accelerator-based ^{99m}Tc production on a routine basis, exploiting the new high-performance cyclotrons now entering into operation

- The still ongoing APOTEMA project as well as the IAEA project launched at international level (CRP code F22062: "Accelerator-based Alternatives to Non-HEU production of Mo-99/Tc-99 m") has demonstrated the feasibility (i.e. physical-chemical constraints) for an accelerator-^{99m}Tc production quality as high as generator-^{99m}Tc.

- All the experience and the knowledge acquired the **APOTEMA group** of people which is expected to be involved into the next **LARAMED project** at LNL , may now be usefully applied to a new step forward…

INFN Istituto Nazionale di Fisica Nucleare Laboratori Nazionali di Legnaro

Research units taking part...

INFN Istituto Nazionale di Fisica Nucleare
Laboratori Nazionali di Legnaro

Università degli Studi di Ferrara
1391
Ex Labore Fructus

INFN Istituto Nazionale di Fisica Nucleare

- Ferrara Branch
- Pavia Branch
- Padua Branch
- Milan Branch
- Bologna Branch

Servizio Sanitario Regionale Emilia-Romagna
Azienda Ospedaliero - Universitaria di Bologna
Alma Mater Studiorum Università di Bologna
Policlinico S. Orsola-Malpighi

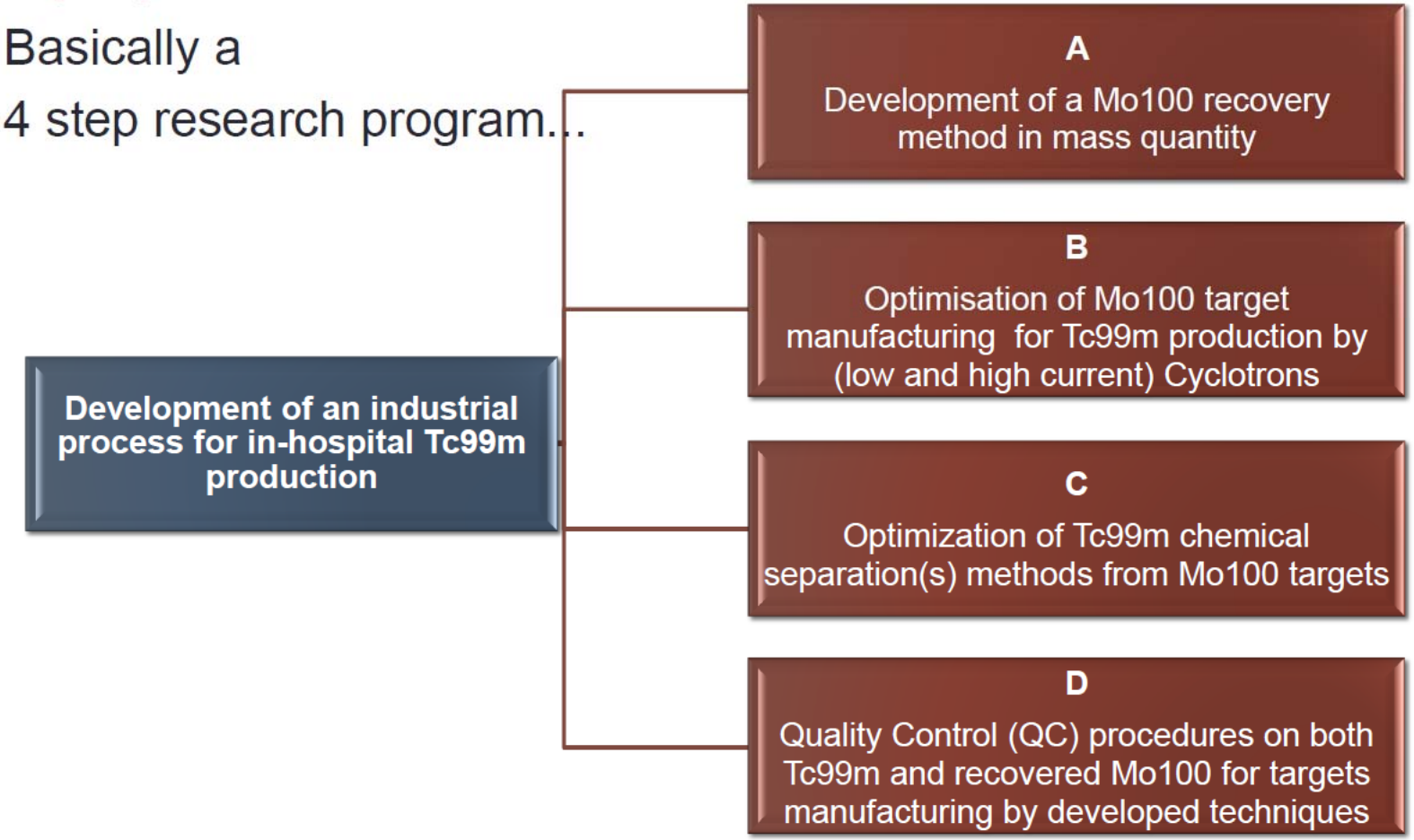
Università degli Studi di Milano

INFN Istituto Nazionale di Fisica Nucleare Laboratori Nazionali di Legnaro

The TECHN-Osp (2015-2017) research project proposal

Basically a

4 step research program...



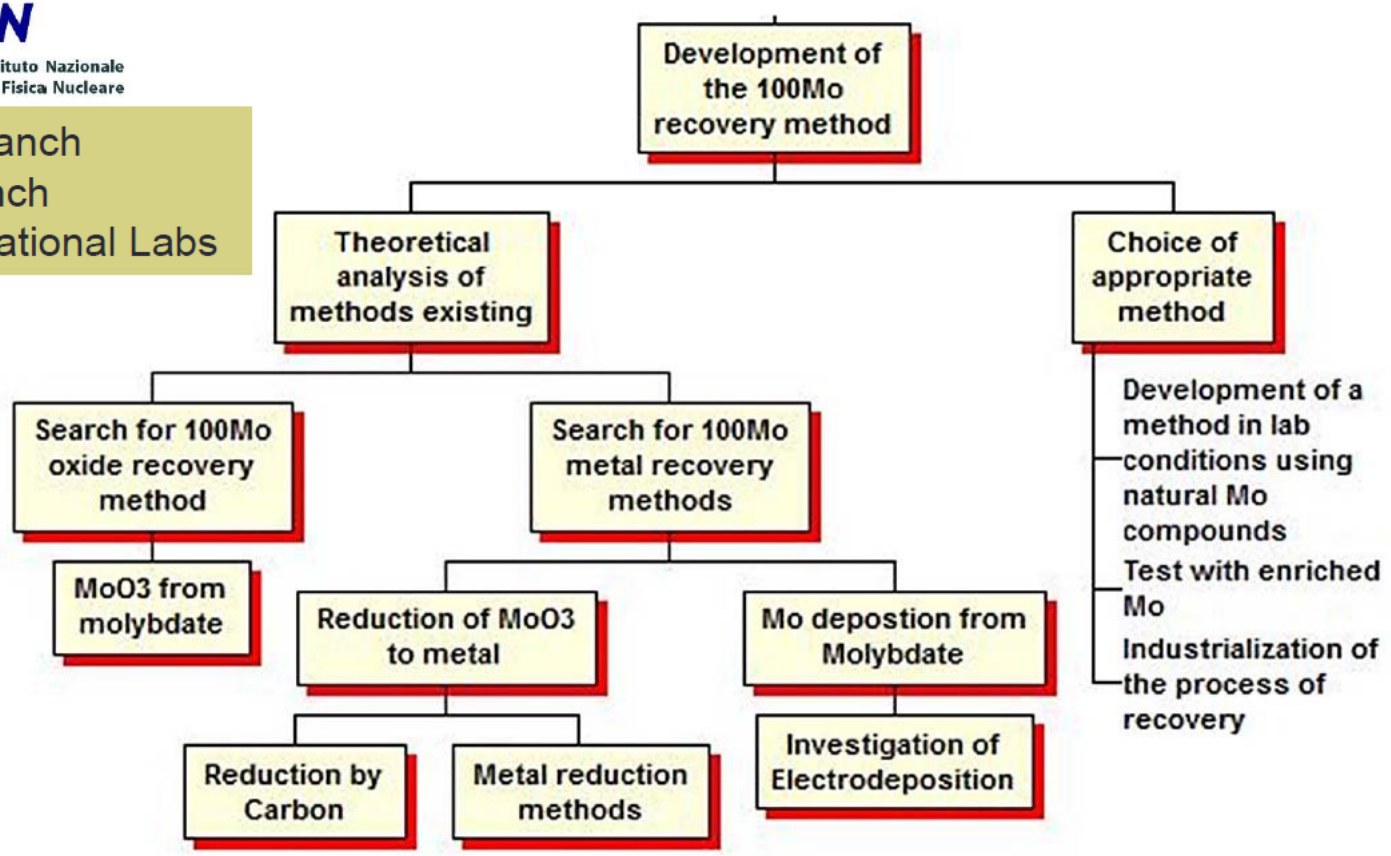
INFN Istituto Nazionale di Fisica Nucleare Laboratori Nazionali di Legnaro

The role of different research units

Step (A): Development of ^{100}Mo recovery method

INFN Istituto Nazionale di Fisica Nucleare

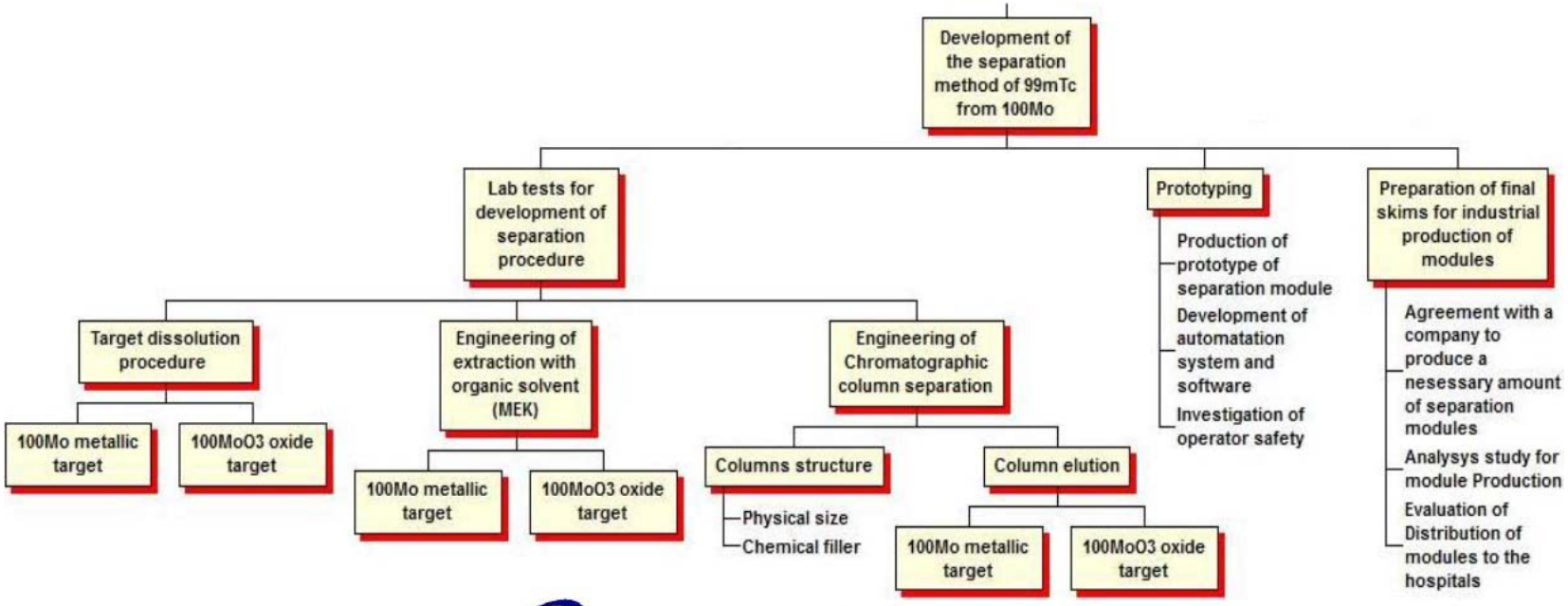
Ferrara branch
Pavia branch
Legnaro national Labs



INFN Istituto Nazionale di Fisica Nucleare
Laboratori Nazionali di Legnaro

The role of different research units

Step (C): Optimization of Tc99m separation(s) methods



UNIVERSITÀ DEGLI STUDI DI FERRARA
EX LABORE FRUCTUS
1391

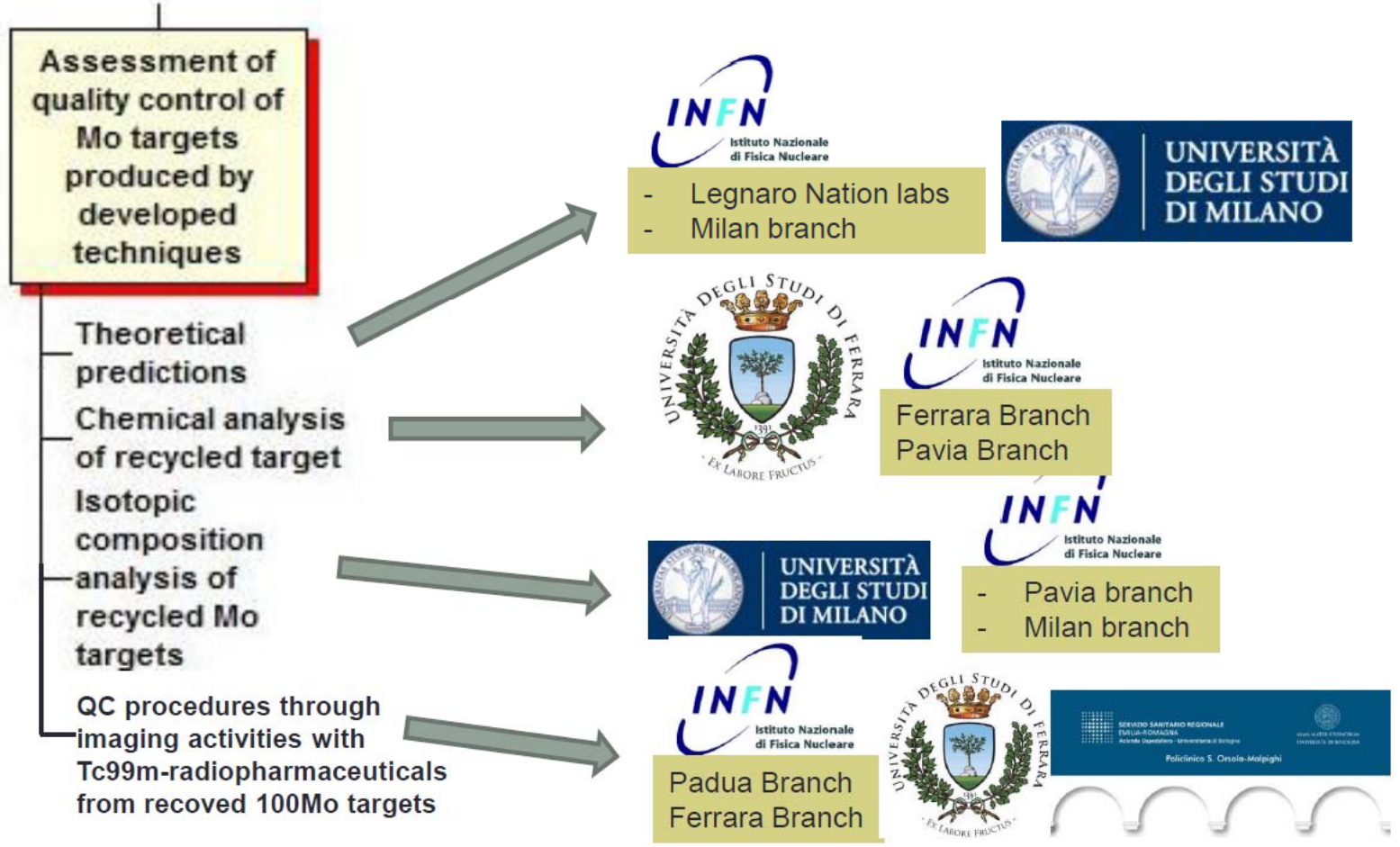
INFN Istituto Nazionale di Fisica Nucleare

- Legnaro National labs
- Pavia branch

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Bologna
Policlinico S. Orsola-Malpighi
ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

The role of different research units

Step (D): Quality Control (QC) procedures on both Tc99m and recovered Mo100



TECHN-Osp project
INFN-Pavia

PLANNED ACTIVITIES scheduled in 2015 and budget quotation (18 K€)

- Studies aimed at **the Optimization of of Tc99m separation(s) methods** with an automated system at high activity levels. Determination of Radiochemical purity **(step C)**
- laboratory chemical studies aimed at the **development of high performance ^{100}Mo recovery method** (Step process A) and separation through the **Automatic Module for high** Tc99m activities (to be performed in collaboration with Ferrara branch)
- Starting Radiochemistry Research activity on a new radioisotope of interest for LARAMED project (in collaboration with Milan Univ. and INFN branch

Item	What is needed	Estimated Cost
1. Products for chemical separation-purification processes	• chemical reagents, • glassware standards, • standards, • exchange resin, • columns, etc. ..	**10.0 k€**
2. Radioactive transport service	• Irradiations to JRC Ispra to LENA Pavia	**2.0 k€**
2. Travels to perform experiments	Domestic between Pavia and Milan, Legnaro, Ferrara, Rome	**2.0 k€**
	international travels (Arronax)	**4.0 k€**

PROGETTO TECHN-Osp

Distribuzione FTE partecipanti al progetto

LNL	FTE
Esposito J.	0.2
Palmieri V.	0.2
Skliarova H.	0.7
Azzolini O.	0.3
Ramones M.	0.8
Rappo S.	1.0
Bello M.	0.8
Uzunov N.	0.5
Melendez L.	0.1
Rosato A.	0.1
	4.7

INFN-Fe	
Gambaccini .M	0.2
Taibi A.	0.2
Di Domenico G.	0.2
Duatti A.	0.5
Pupillo G.	1.0
Uccelli L.	0.5
Pasquali M.	1.0
Boschi A.	1.0
Giganti M.	0.5
Martini P.	1.0
	6.1

INFN-Mi	FTE
Groppi F.	0.8
Bonardi M.	1.0
Manenti S.	1.0
Gini L.	0.5
Bazzocchi A.	0.8
	4.1

INFN-Pd	FTE
De Nardo L.	0.2
Sartori P.	0.2
	0.4

INFN-Pv	FTE
Salvini A.	0.3
Oddone M.	0.5
Prata M.	0.3
Magrotti G.	0.3
Strada L.	0.8
	2.2

INFN-Bo	FTE
Marengo M.	0.2
Cocoria G.	0.3
????	
	0.5

TOTALE FTE 18.0