UNIVERSITY OF CAMBRIDGE

Engineering Design Centre

SIEMENS

A compact, low-energy accelerator for medical radioisotope production — yields and isotopic purity

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Contents

- The needs of nuclear medicine
- The challenges
- A low-energy, compact solution
- Current findings
- Future prospects

Radionuclides in nuclear medicine

- A large range of radionuclides are utilised in nuclear medicine (NM)

Diagnostic imaging		
SPECT	^{67}Ga, ^{81m}Kr, **^{99m}Tc**, ^{111}In, ^{123}I, ^{133}Xe, ^{201}Tl, ^{131}I, ^{177}Lu	
PET	**Short-lived**	**Long-lived**
	^{11}C, ^{13}N, ^{15}O, **^{18}F**, ^{68}Ga, ^{82}Rb	^{44}Sc, ^{64}Cu, ^{76}Br, ^{86}Y, ^{89}Zr, ^{124}I
Radiotherapy		
β^- emitters	^{32}P, ^{89}Sr, ^{90}Y, ^{131}I, ^{153}Sm, ^{166}Ho, ^{177}Lu, ^{169}Er, ^{186}Re, ^{188}Re	
α emitters	^{212}Pb, ^{212,213}Bi, ^{211}At, ^{223,224}Ra, ^{225}Ac, ^{227}Th, ^{230}U	

- Nuclear medicine is dominated by ^{99m}Tc
  - Used in approximately 75-85% of all diagnostic scans in NM
  - Its dominance arose from its availability and utility

The challenges

- There have been serious shortages in supply
  - *Unexpected shut-downs of the National Research Universal (NRU) reactor in Canada and the High Flux Reactor (HFR) in the Netherlands (2008-2010)*
    - *Reduced available* ^{99m}*Tc supply by ~70%*
    - *Nuclear medicine 'brought to a standstill overnight!'*
  - *More shortages are expected, as aging research reactors are closing with uncertainty still surrounding their replacement*

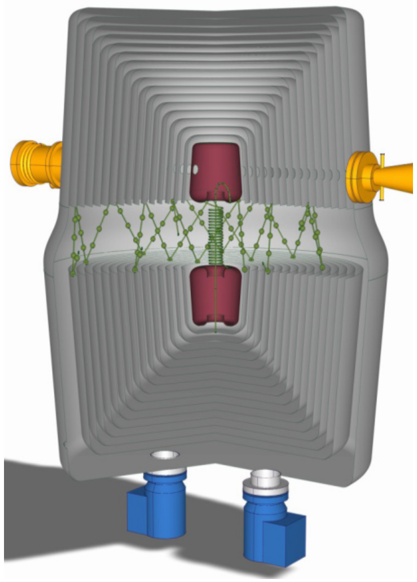
The industry needs **security of supply** to continue growing confidently

- As the uptake and needs of nuclear medicine expand and diversify
  - *Production of current isotopes **must** increase*
  - *Range of available isotopes **must** expand*

How can we provide this increased availability?

A low-energy, compact solution?

- In collaboration with the STFC, Siemens are developing a particle accelerator for radionuclide production
  - *A novel, compact DC electrostatic accelerator based on the original Cockcroft-Walton design*
  - *High current (**10 MeV protons, 5 MeV deuterons, ~5 mA**)*
  - *Spatial foot print of < 2 m^2*
  - *Multiple beam lines*



A localised production system?

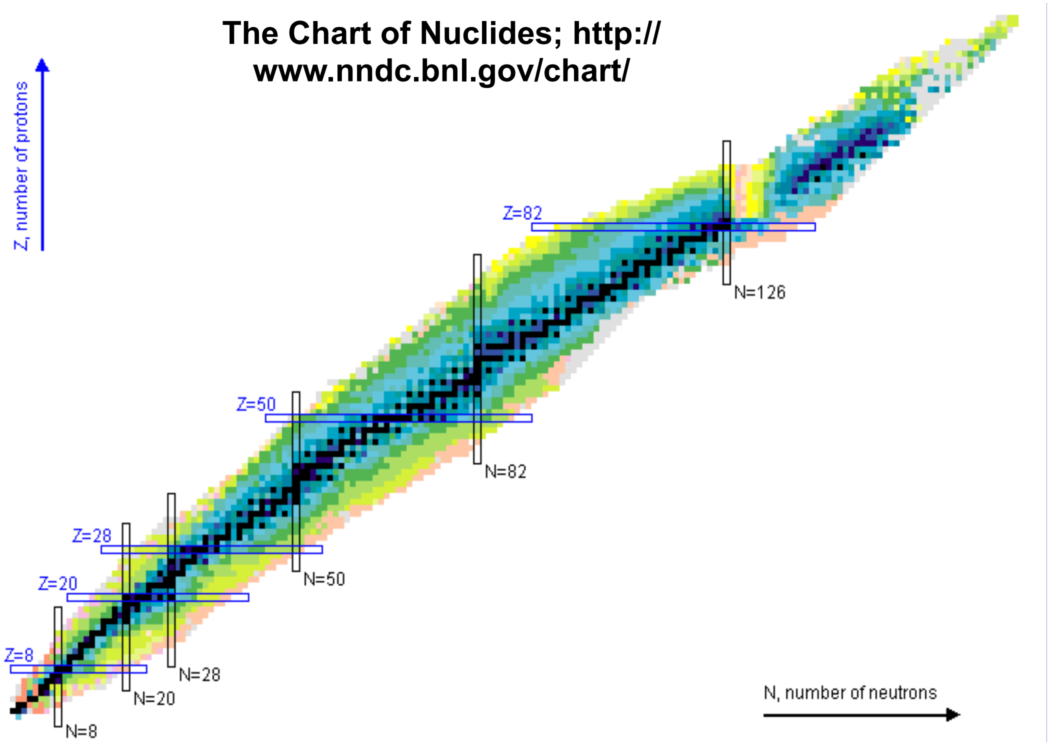
- Rather than rely solely on a centralised production system, could we produce more radionuclides **locally**?
  - One production facility would provide for a small number of hospitals
  - Radionuclides could be produced **on-site**, on-demand, minimal transportation
  - Easier to obtain new and novel radionuclides
    - Shorter-lived radionuclides to increase patient throughput
    - Offer new diagnostic and therapeutic techniques

- What would be the requirements on such a system?
  - Produces sufficient quantities of medically important radionuclides
  - High elemental and isotopic purity
  - Ease of operation
  - Low cost of ownership

Computational methods for assessing low-energy production

- Programs such as **TALYS**, **EMPIRE** and **ALICE/ASH** can be used to generate ‘excitation functions’ or cross-sections

- *In this work **TALYS (v1.6)**, and **SRIM** have been used*
- *Estimates have been made of the radionuclidic yields from a reaction*
  - Target isotope
  - Isotopic and elemental impurities


The Chart of Nuclides; http://www.nndc.bnl.gov/chart/

Theoretical calculations – some words of caution...

- TALYS is not always accurate
  - *Cross-sections usually compare well to experimental data*
    - Experimental data not always available
      - Unwanted side-reaction e.g. p,2n or p,3n, reactions are particularly problematic
    - Sometimes considerable conflict between experimental data sets e.g. ^{100}Mo(p,2n)

  - *Predicted yields—even those based on experimental cross-sections—still vary from experimental yields*
    - Some have commented that "yield does not scale linearly with current"

  - *Sometimes TALYS does strange things....*

What radionuclides have been assessed?

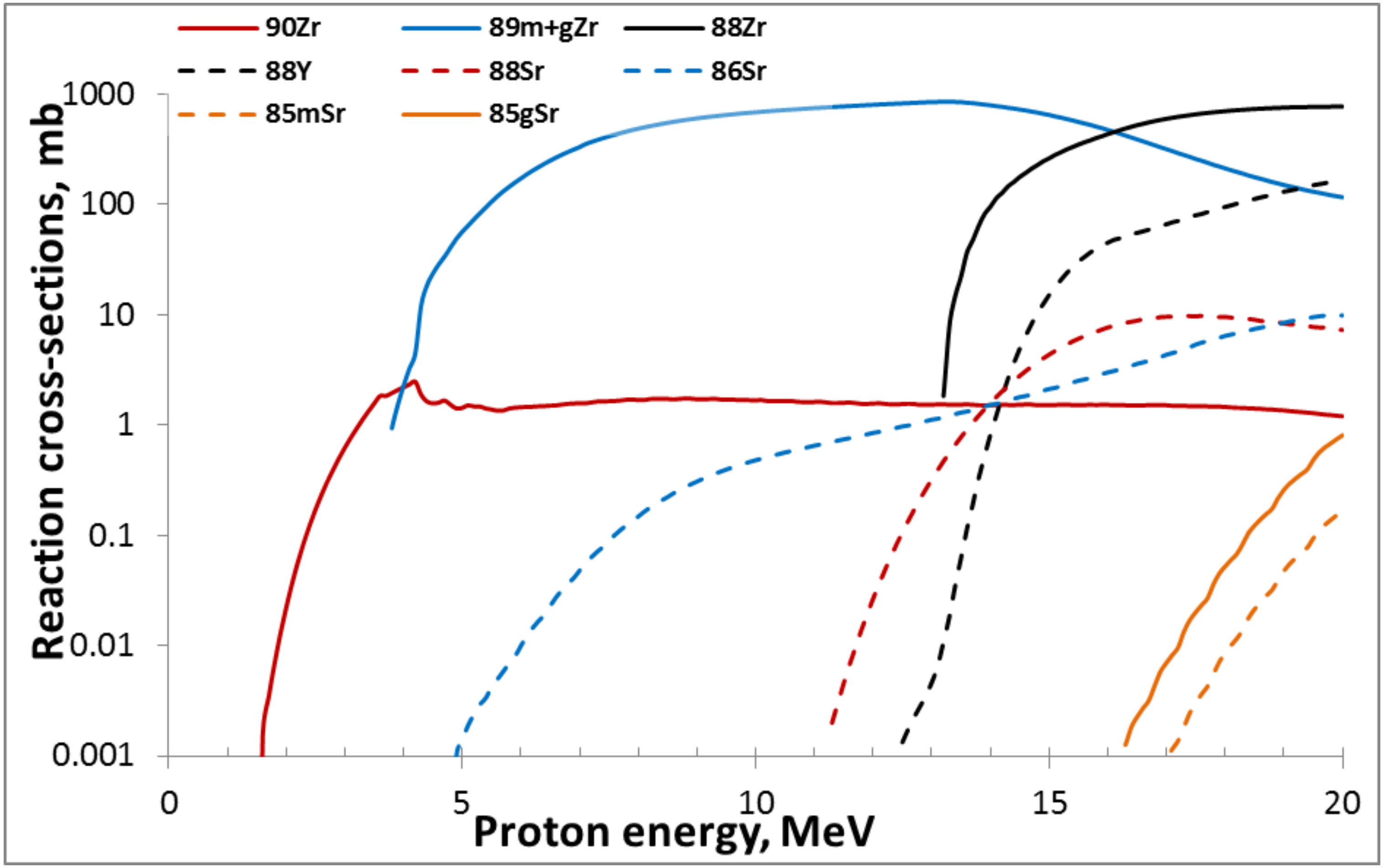
- *The production of several different isotopes have been considered, with a main focus on the following*

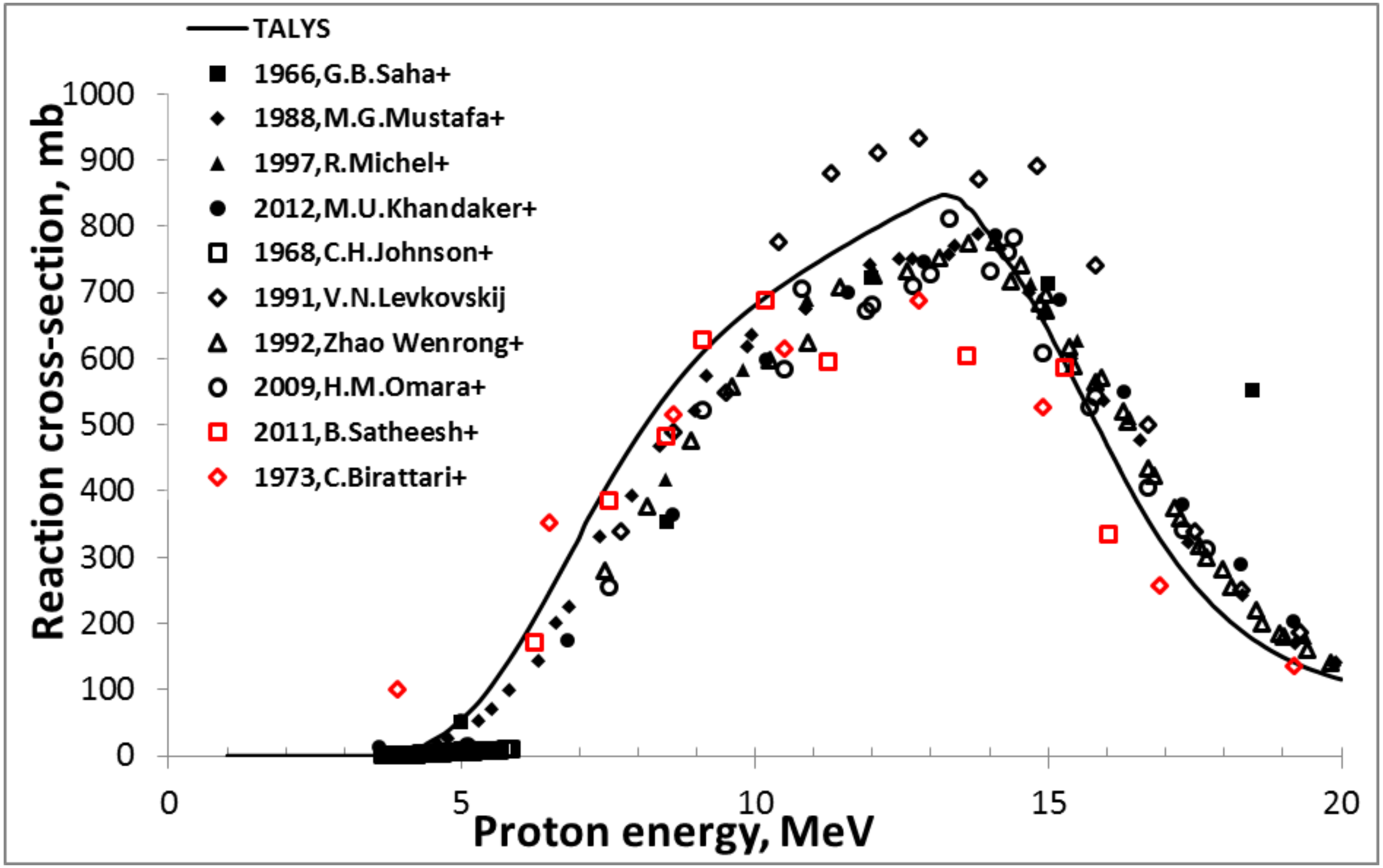
^{89}Zr

- **PET** isotope, half-life of 78.41 hrs
  - Longer half-life makes it ideal for labelling monoclonal antibodies (mAbs) for immunoPET

Results

- Considered the ^{89}Y(p,n) reaction
  - Ep = 10→4 MeV, 1 hr irradiation at 1 mA
- Could produce up to 320 mCi
- Avoids production of long-lived ^{88}Zr, recently identified as a significant impurity at higher energies


90Zr
89m+gZr
88Zr
88Y
88Sr
86Sr
85mSr
85gSr
Reaction cross-sections, mb
1000
100
10
1
0.1
0.01
0.001
0
5
10
15
20
Proton energy, MeV

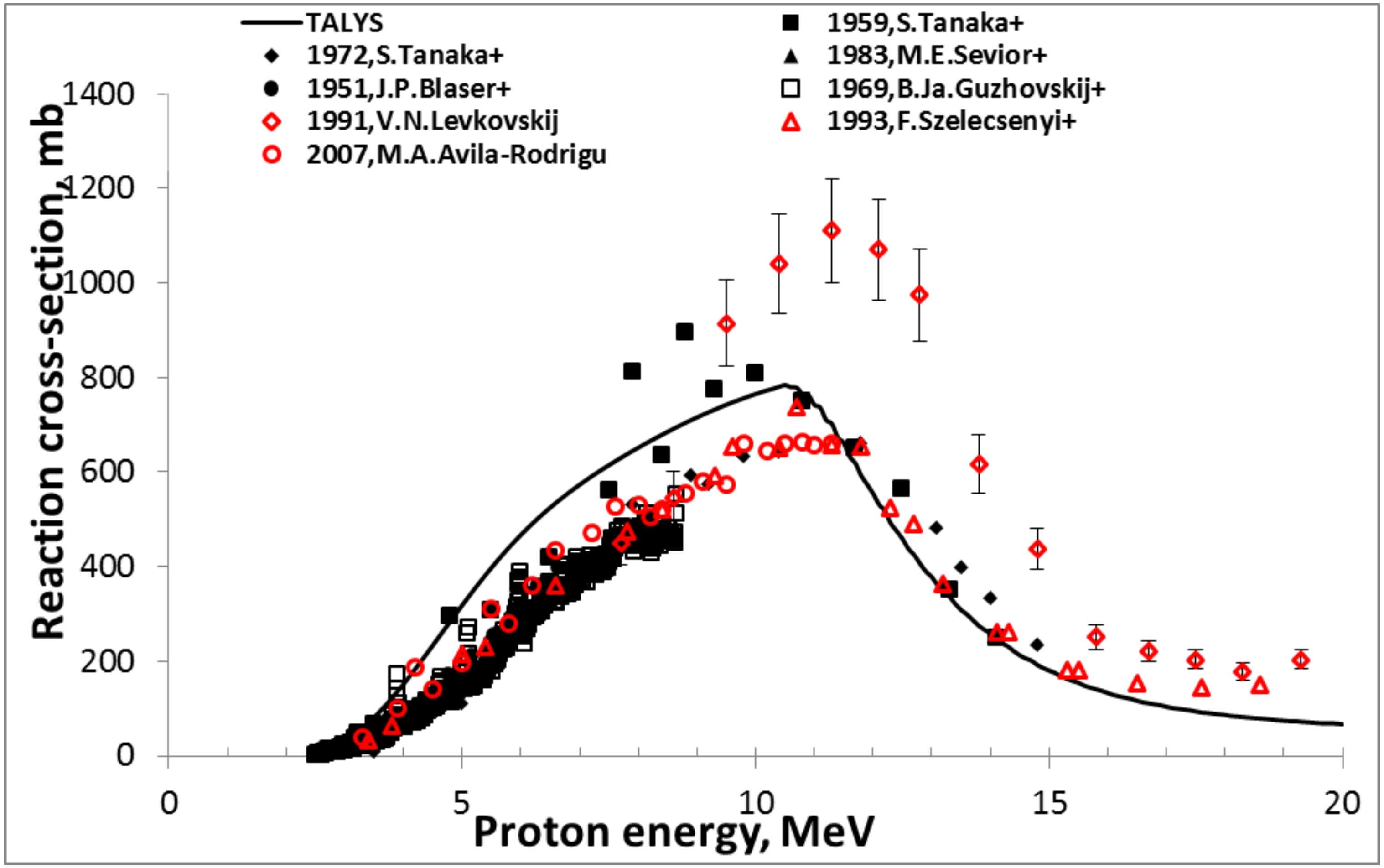

TALYS
1966,G.B.Saha+
1988,M.G.Mustafa+
1997,R.Michel+
2012,M.U.Khandaker+
1968,C.H.Johnson+
1991,V.N.Levkovskij
1992,Zhao Wenrong+
2009,H.M.Omara+
2011,B.Satheesh+
1973,C.Birattari+
Reaction cross-section, mb
1000
900
800
700
600
500
400
300
200
100
0
0
5
10
15
20
Proton energy, MeV

^{64}Cu

- Decays by β^- (38.5%) and β^+ (17.6%), half-life of 12.7 hrs
  - **Dual functionality** radioisotope
    - PET and radiotherapy

Results

- Considered the ^{64}Ni(p,n) reaction
  - Ep = 10→3 MeV, 1 hr irradiation at 1 mA
  - 99.32% target enrichment
- Could produce up to 8000 mCi
- Avoids co-production of the stable ^{63}Cu

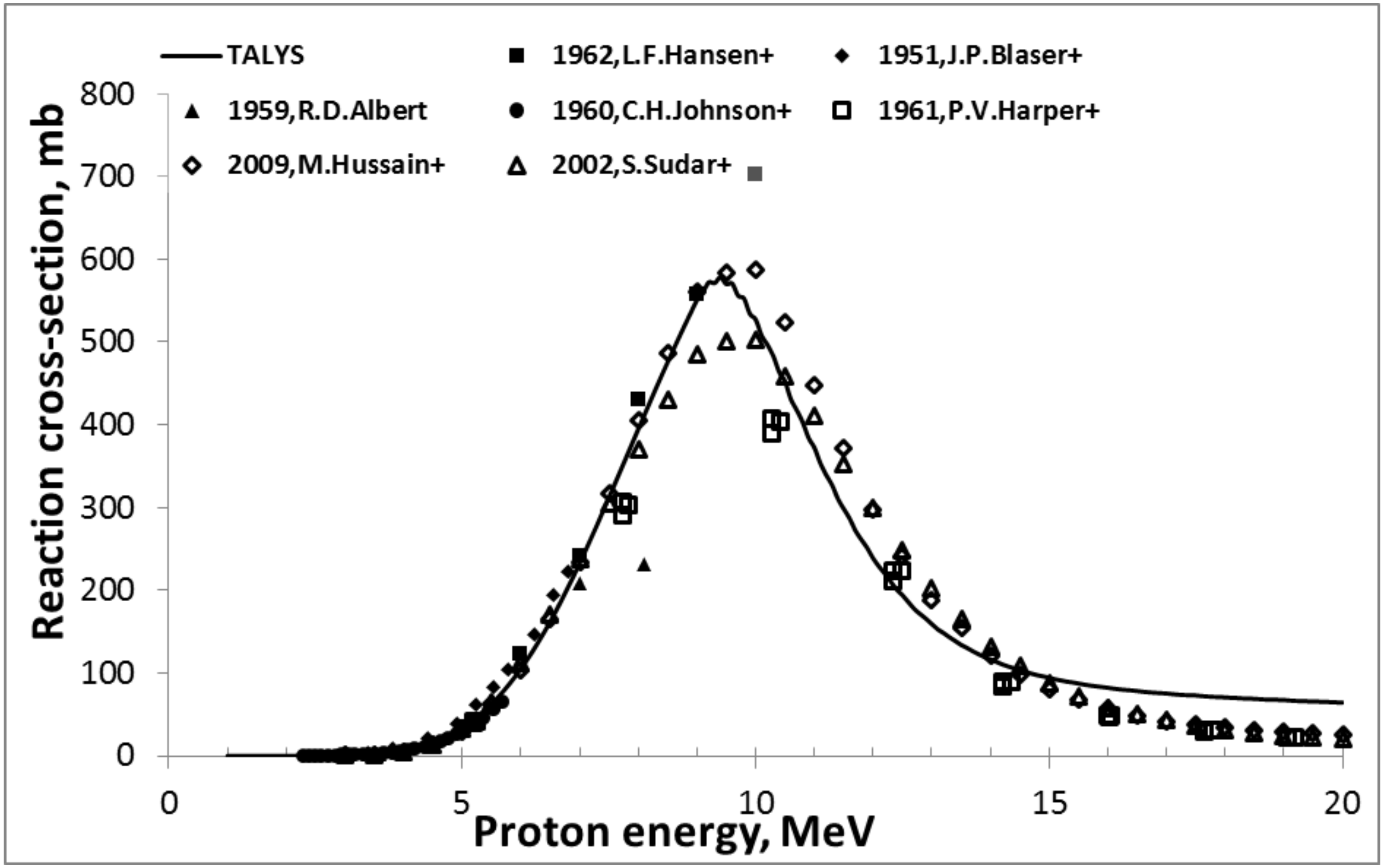

TALYS
1972,S.Tanaka+
1951,J.P.Blaser+
1991,V.N.Levkovskij
2007,M.A.Avila-Rodrigu
1959,S.Tanaka+
1983,M.E.Sevior+
1969,B.Ja.Guzhovskij+
1993,F.Szelecsenyi+
Reaction cross-section, mb
1400
1200
1000
800
600
400
200
0
0
5
10
15
20
Proton energy, MeV

^{103}Pd

- Radiotherapy isotope, half-life of 16.991 days
  - Decays primarily by electron capture

Results

- Considered the ^{103}Rh(p,n) reaction
    - Ep = 10→5 MeV, 1 hr irradiation at 1 mA
- Can produce up to 98 mCi
- Some co-production of the stable ^{102}Pd which reduces the radioisotopic purity
    - Reduction in beam energy can reduce/eliminate production, at the cost of activity

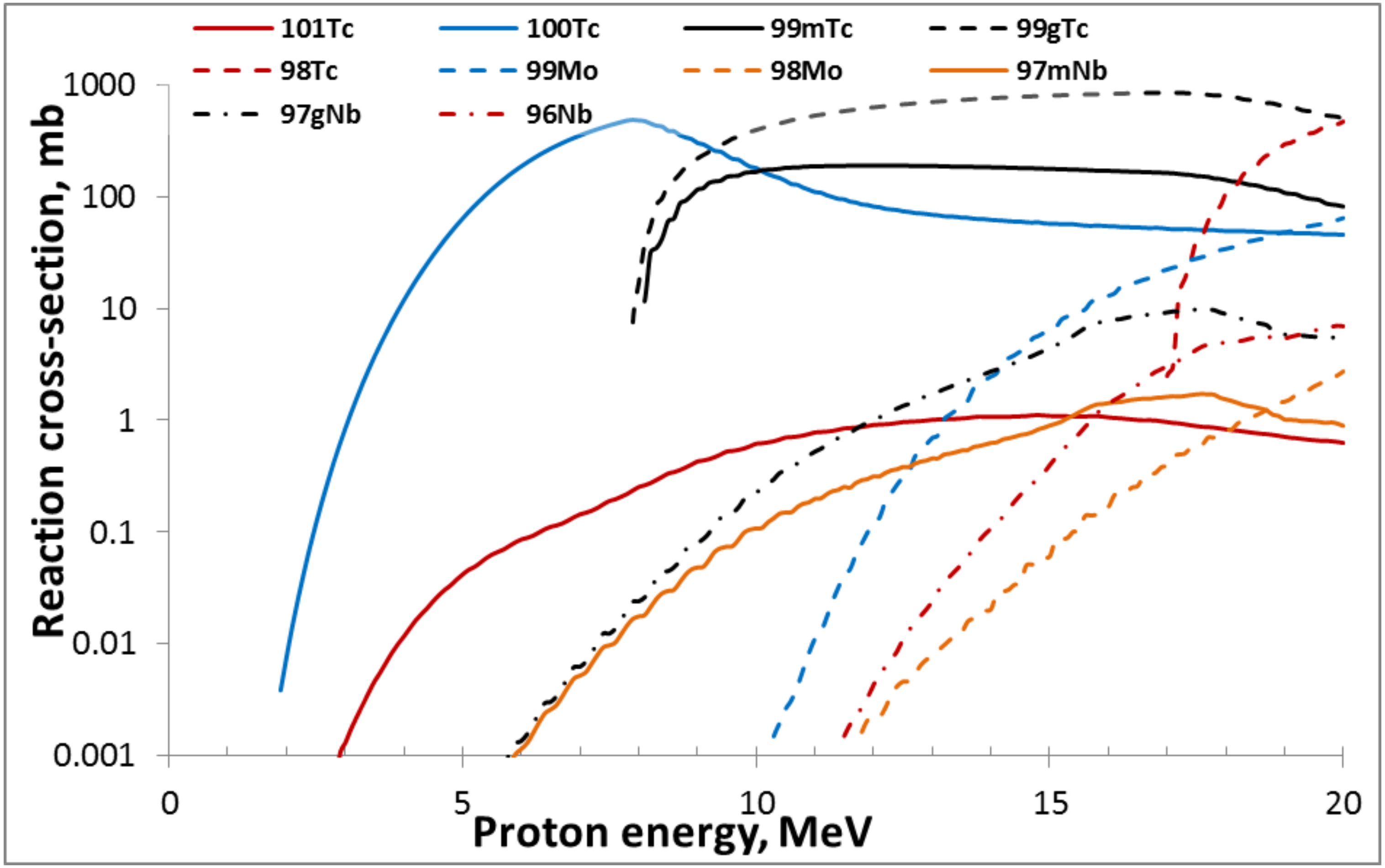

TALYS
■ 1962,L.F.Hansen+
◆ 1951,J.P.Blaser+
▲ 1959,R.D.Albert
● 1960,C.H.Johnson+
□ 1961,P.V.Harper+
◇ 2009,M.Hussain+
△ 2002,S.Sudar+
Reaction cross-section, mb
800
700
600
500
400
300
200
100
0
0
5
10
15
20
Proton energy, MeV

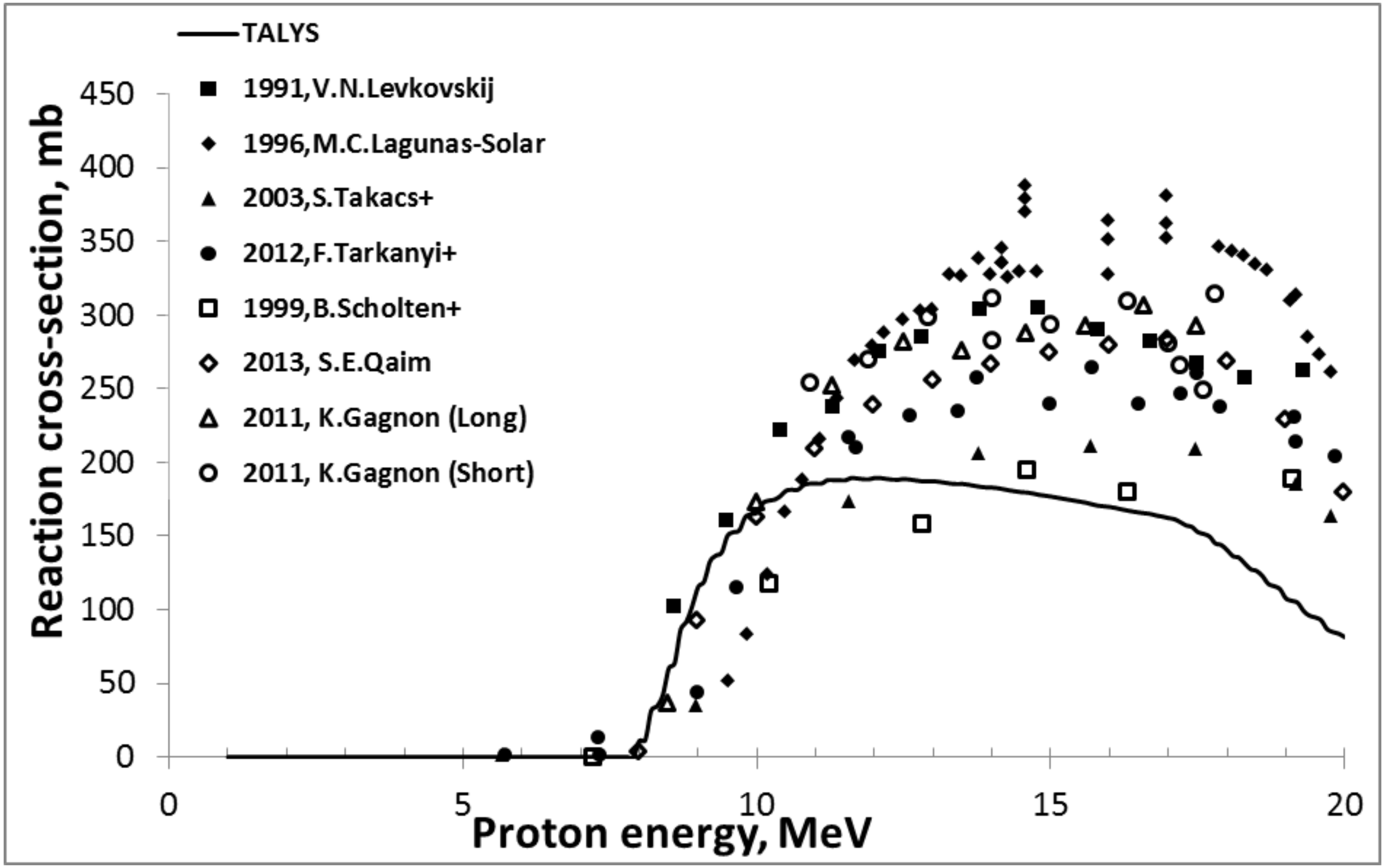
^{99m}Tc

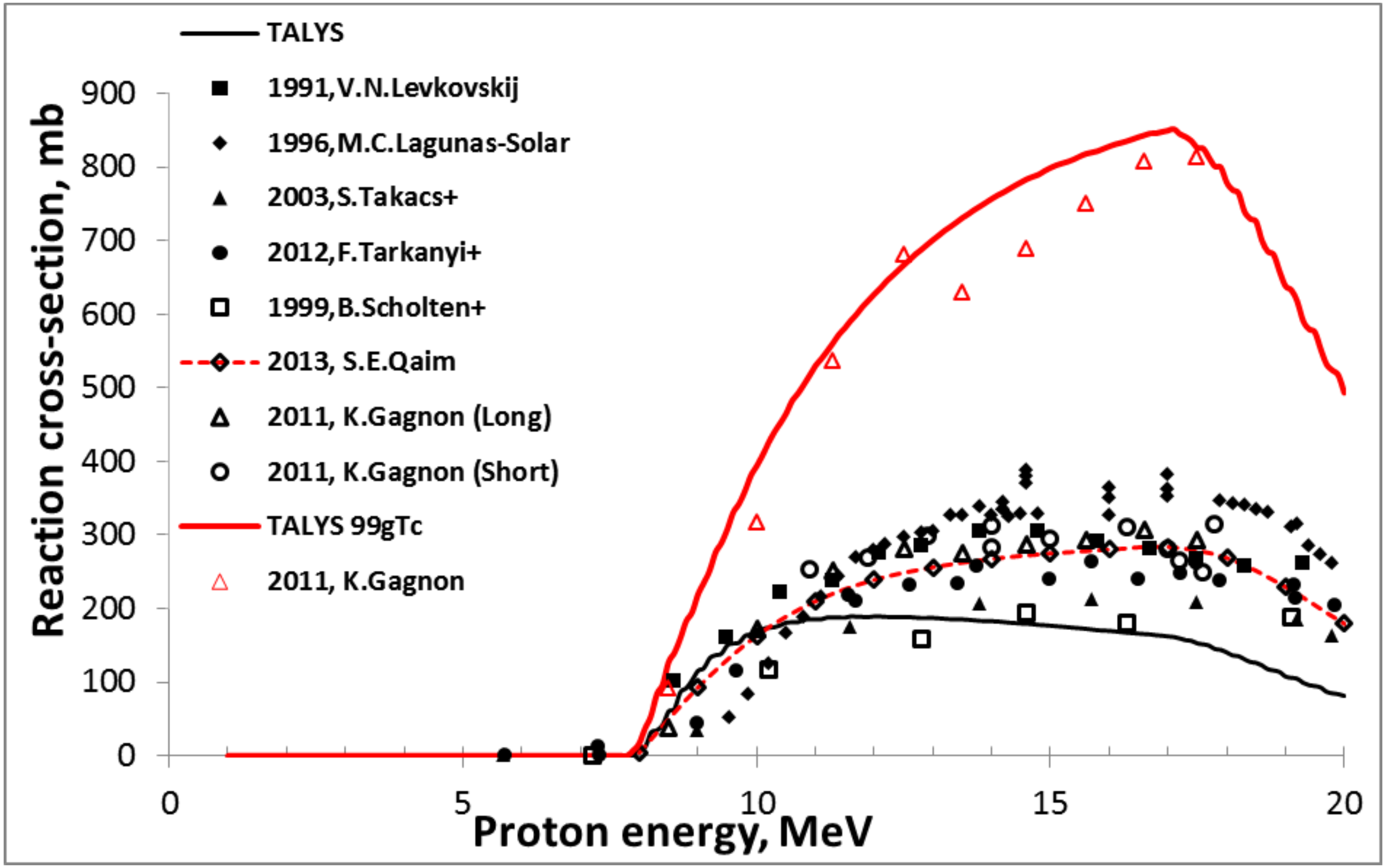
- SPECT isotope, half-life of 6 hrs

Results

- Considered the ^{100}Mo(p,2n) reaction
  - Ep = 10→8 MeV, 1 hr irradiation at 1 mA
- Can produce up to 900 mCi
- Avoid co-production of long-lived ^{98}Tc
- Primary impurity is the isomeric state ^{99g}Tc
  - 2:1 ratio of ^{99g}Tc to ^{99m}Tc
  - Better than at higher energy irradiation


101Tc
100Tc
99mTc
99gTc
98Tc
99Mo
98Mo
97mNb
97gNb
96Nb
Reaction cross-section, mb
1000
100
10
1
0.1
0.01
0.001
0
5
10
15
20
Proton energy, MeV


TALYS
■ 1991,V.N.Levkovskij
◆ 1996,M.C.Lagunas-Solar
▲ 2003,S.Takacs+
● 2012,F.Tarkanyi+
□ 1999,B.Scholten+
◇ 2013, S.E.Qaim
△ 2011, K.Gagnon (Long)
○ 2011, K.Gagnon (Short)
Reaction cross-section, mb
450
400
350
300
250
200
150
100
50
0
0
5
10
15
20
Proton energy, MeV


TALYS
1991,V.N.Levkovskij
1996,M.C.Lagunas-Solar
2003,S.Takacs+
2012,F.Tarkanyi+
1999,B.Scholten+
2013, S.E.Qaim
2011, K.Gagnon (Long)
2011, K.Gagnon (Short)
TALYS 99gTc
2011, K.Gagnon
Reaction cross-section, mb
900
800
700
600
500
400
300
200
100
0
0
5
10
15
20
Proton energy, MeV

What other radionuclides do we know can be produced?

- *Short-lived PET radionuclides*
  - ^{18}F, ^{15}O, ^{13}N, ^{11}C
  - Are already/can be produced from accelerators using protons and deuterons in the applicable energy range

What does this mean for the Siemens accelerator?

- *These yields would be suitable for a localised radionuclide production system*
  - Sufficient for supplying a small hospital/nuclear medicine facility
  - Longer irradiation times/higher currents can cater for larger/more facilities
  - Beam splitting would allow for production of multiple nuclides simultaneously

- *Localised production can offer*
  - Simplified infrastructure
  - Greater nuclear medicine flexibility
  - Increased patient throughput through use of shorter half-life isotopes

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Any questions?

Alternatively...

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