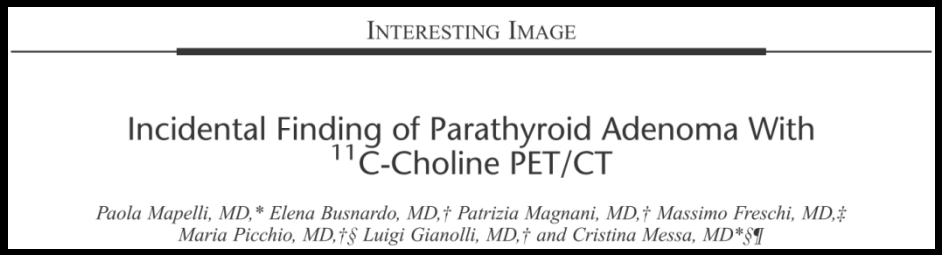
Choline PET Imaging of Hyperparathyroidism – Fulfill the Unmet Needs, ?

花蓮慈濟醫院核子醫學科

陳昱宏

Fluorocholine marketing (2010)

Prostate CA & HCC

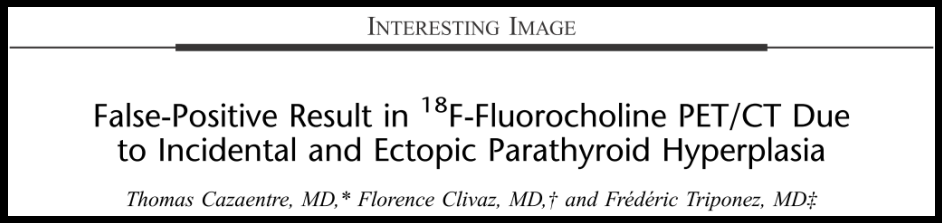


INTERESTING IMAGE

Incidental Finding of Parathyroid Adenoma With ^{11}C-Choline PET/CT

Paola Mapelli, MD, Elena Busnardo, MD,† Patrizia Magnani, MD,† Massimo Freschi, MD,‡ Maria Picchio, MD,†§ Luigi Gianolli, MD,† and Cristina Messa, MD*§¶*

Clin Nucl Med. 2012 Jun;37(6):593-5.



INTERESTING IMAGE

False-Positive Result in ^{18}F-Fluorocholine PET/CT Due to Incidental and Ectopic Parathyroid Hyperplasia

Thomas Cazaentre, MD, Florence Clivaz, MD,† and Frédéric Triponez, MD‡*

Clin Nucl Med. 2014 Jun;39(6):e328-30.

Fluciclovine (2016)

PSMA theranostics

FAPI

etc…

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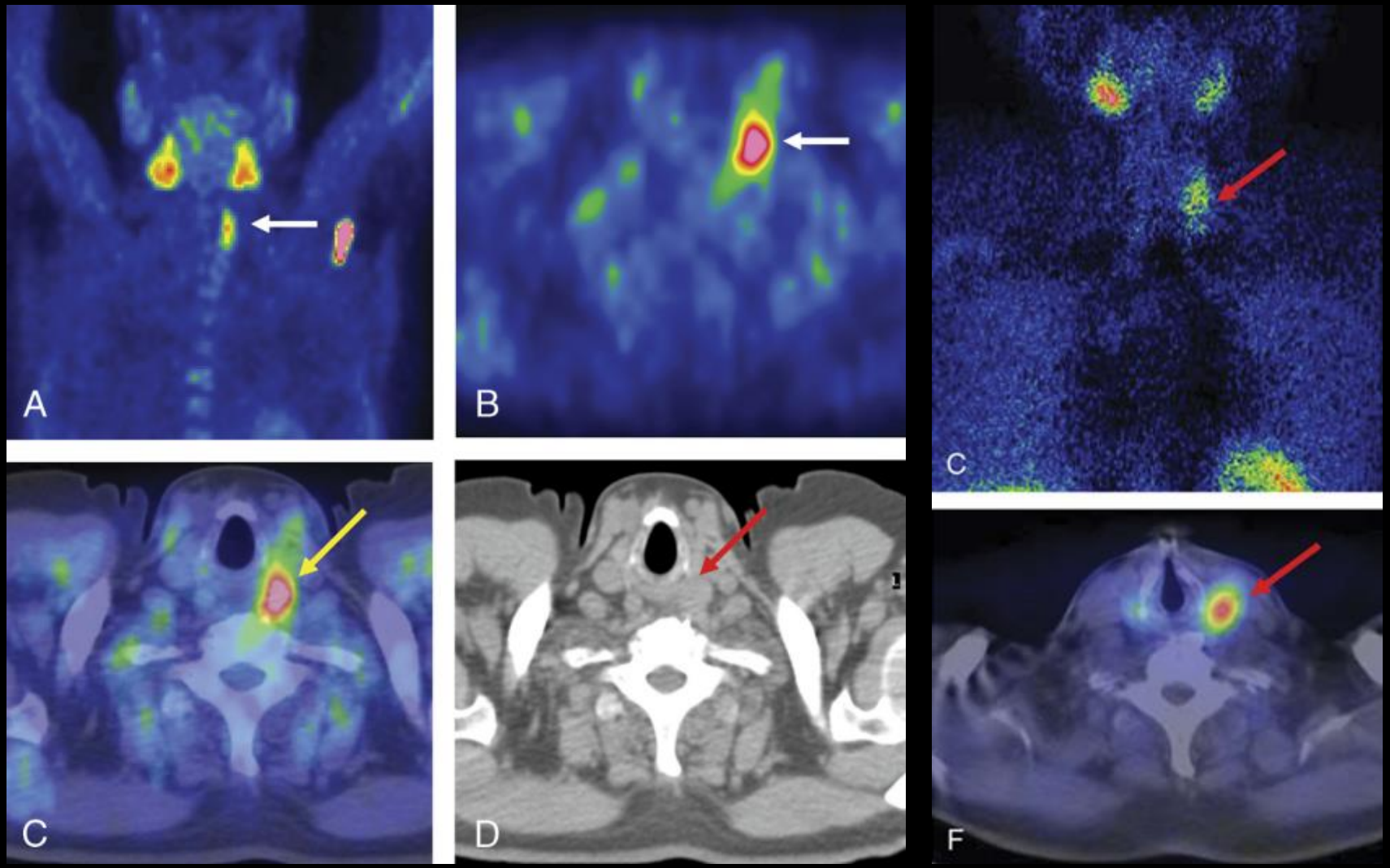

Clin Nucl Med. 2012 Jun;37(6):593-5.

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1. Parathyroid Glands Hyperplasias Mimicking Medullary Thyroid Carcinoma Metastatic Lymph Nodes on 18F-DOPA PET/CT.
Terroir M, Grimaldi S, Hartl D, Leboulleux S, Deandreis D.
Clin Nucl Med. 2019 Aug;44(8):e497-e498. doi: 10.1097/RLU.0000000000002633.
PMID: 31274634
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2. Optimization of parathyroid ^{11}C-choline PET protocol for localization of parathyroid adenomas in patients with primary hyperparathyroidism.
Noltes ME, Kruijff S, Noordzij W, Telenga ED, Vállez García D, Trofimiuk-Müldner M, Opalińska M, Hubalewska-Dydejczyk A, Luurtsema G, Dierckx RAJO, El Moumni M, Boellaard R, Brouwers AH.
EJNMMI Res. 2019 Jul 31;9(1):73. doi: 10.1186/s13550-019-0534-5.
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3. 64CuCl2 PET/CT in a Hyperfunctioning Parathyroid Gland.
Evangelista L, Trevisan M, Sepulcri M.
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Terroir M, Grimaldi S, Hartl D, Leboulleux S, Deandreis D.
Clin Nucl Med. 2019 Jun 1. doi: 10.1097/RLU.0000000000002633. [Epub ahead of print]
PMID: 31162251
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5. Usefulness of 18F-Fluorocholine Positron Emission Tomography-Computed Tomography in Locating Lesions in Hyperparathyroidism: A Systematic Review.
Boccalatte LA, Higuera F, Gómez NL, de la Torre AY, Mazzaro EL, Galich AM, Collaud C, Figari MF.
JAMA Otolaryngol Head Neck Surg. 2019 May 30. doi: 10.1001/jamaoto.2019.0574. [Epub ahead of print]

Michaud L, Burgess A, Huchet V, Lefevre M, Tassart M, Ohnona J, Kerrou K, Balogova S, Talbot JN, Périé S.
J Clin Endocrinol Metab. 2014 Dec;99(12):4531-6. doi: 10.1210/jc.2014-2821.
PMID: 25215560
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54. ^{18}F-Fluorocholine PET/CT for localization of hyperfunctioning parathyroid tissue in primary hyperparathyroidism: a pilot study.
Lezaic L, Rep S, Sever MJ, Kocjan T, Hocevar M, Fettich J.
Eur J Nucl Med Mol Imaging. 2014 Nov;41(11):2083-9. doi: 10.1007/s00259-014-2837-0. Epub 2014 Jul 26.
PMID: 25063039
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55. False-positive result in 18F-fluorocholine PET/CT due to incidental and ectopic parathyroid hyperplasia.
Cazaentre T, Clivaz F, Triponez F.
Clin Nucl Med. 2014 Jun;39(6):e328-30. doi: 10.1097/RLU.0b013e3182a77b62.
PMID: 24152627
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56. F18-choline, a novel PET tracer for parathyroid adenoma?
Quak E, Lheureux S, Reznik Y, Bardet S, Aide N.
J Clin Endocrinol Metab. 2013 Aug;98(8):3111-2. doi: 10.1210/jc.2013-2084. Epub 2013 Jun 20. No abstract available.
PMID: 23788686
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57. Incidental finding of parathyroid adenoma with 11C-choline PET/CT.
Mapelli P, Busnardo E, Magnani P, Freschi M, Picchio M, Gianolli L, Messa C.
Clin Nucl Med. 2012 Jun;37(6):593-5. doi: 10.1097/RLU.0b013e31824c5ffc.
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- ✓ Choline PET & hyperparathyroidism – The Evidence
- Image protocol, Refined
- Unmet needs? Have we figured all them out?
- Questions not yet addressed?

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Choline PET Imaging of Hyperparathyroidism – The Evidence

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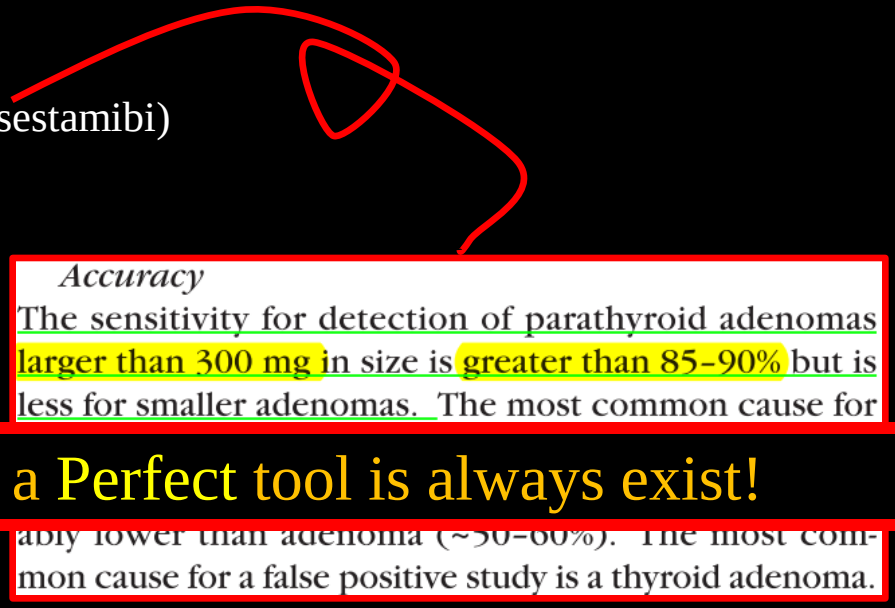
Parathyroid Imaging

- Less or minimal invasive parathyroidectomy
- Primary hyperparathyroidism
- Pre-operative localization (old-school)
  - Ultrasound (US) of the neck
  - Radionuclide images (Tc-99m sestamibi)
- Intra-operative iPTH test



Accuracy

The sensitivity for detection of parathyroid adenomas larger than 300 mg in size is greater than 85–90% but is less for smaller adenomas. The most common cause for

ably lower than adenoma (~50–60%). The most common cause for a false positive study is a thyroid adenoma.

The Quest for seeking a Perfect tool is always exist!

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Fluorocholine marketing (2010)

Incidental Finding of Parathyroid Adenoma With ^{11}C-Choline PET/CT

Clin Nucl Med. 2012 Jun;37(6):593-5.

False-Positive Result in ^{18}F-Fluorocholine PET/CT Due to Incidental and Ectopic Parathyroid Hyperplasia

Clin Nucl Med. 2014 Jun;39(6):e328-30.

	PET/CT	SPECT/CT	Subtraction	Dual-phase	Combined
All patients (24 patients, 39 lesions)					
Sensitivity (%)	92	49*,***	46*,***	44*,***	64***
Specificity (%)	100	100	100	100	100
Accuracy (%)	98	83	82	82	88
PPV (%)	100	100	100	100	100
NPV (%)	96	80	79	79	85

Eur J Nucl Med Mol Imaging. 2014 Nov;41(11):2083-9.

	Patient-based sensitivity	Lesion-based sensitivity	Lesion-based specificity	Lesion-based accuracy
US open reading	8/16 = 50%	12/24 = 50%	3/9 = 33%	15/33 = 46%
^{99m}Tc-sestamibi/^{123}I open reading	15/16 = 94%	20/24 = 83%	5/9 = 56%	25/33 = 76%
^{99m}Tc-sestamibi/^{123}I masked reading	15/16 = 94%	20/24 = 83%	5/9 = 56%	25/33 = 76%
FCH-PET/CT open reading	15/16 = 94%	23/24 = 96%	8/9 = 88%	31/33 = 94%
FCH-PET/CT masked reading	15/16 = 94%	23/24 = 96%	5/9 = 56%	28/33 = 85%

Medicine (Baltimore). 2015 Oct;94(41):e1701.

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Fluorocholine marketing (2010)

Eur J Nucl Med Mol Imaging. 2014 Nov;41(11):2083-9.
Medicine (Baltimore). 2015 Oct;94(41):e1701.

Pilot studies

Table 5 Lesion-based sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of each imaging modality based on true-positive, true-negative, false-positive and false-negative results

imaging modality	True-positive	True-negative	False-positive	False-negative	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
^{18}F-Fluorocholine PET/CT	74	190	8	5	93.7	96.0	90.2	97.4	95.3
^{99m}Tc-MIBI/tetrofosmin SPECT/CT	48	195	3	31	60.8	98.5	94.1	86.3	87.7

Table 3 Histopathological findings (size and weight) in parathyroid adenomas from PET/CT-positive and SPECT/CT-positive patients and PET/CT-positive and SPECT/CT-negative patients

Histopathological findings	PET/CT-positive and SPECT/CT-positive	PET/CT-positive and SPECT/CT-negative	*p* value
Size (mm), mean ± SD	17.6 ± 7.4 (n = 47)	13.0 ± 6.6 (n = 23)	0.013
Weight (g), mean ± SD	2.09 ± 1.89 (n = 34)	1.24 ± 1.38 (n = 17)	0.106

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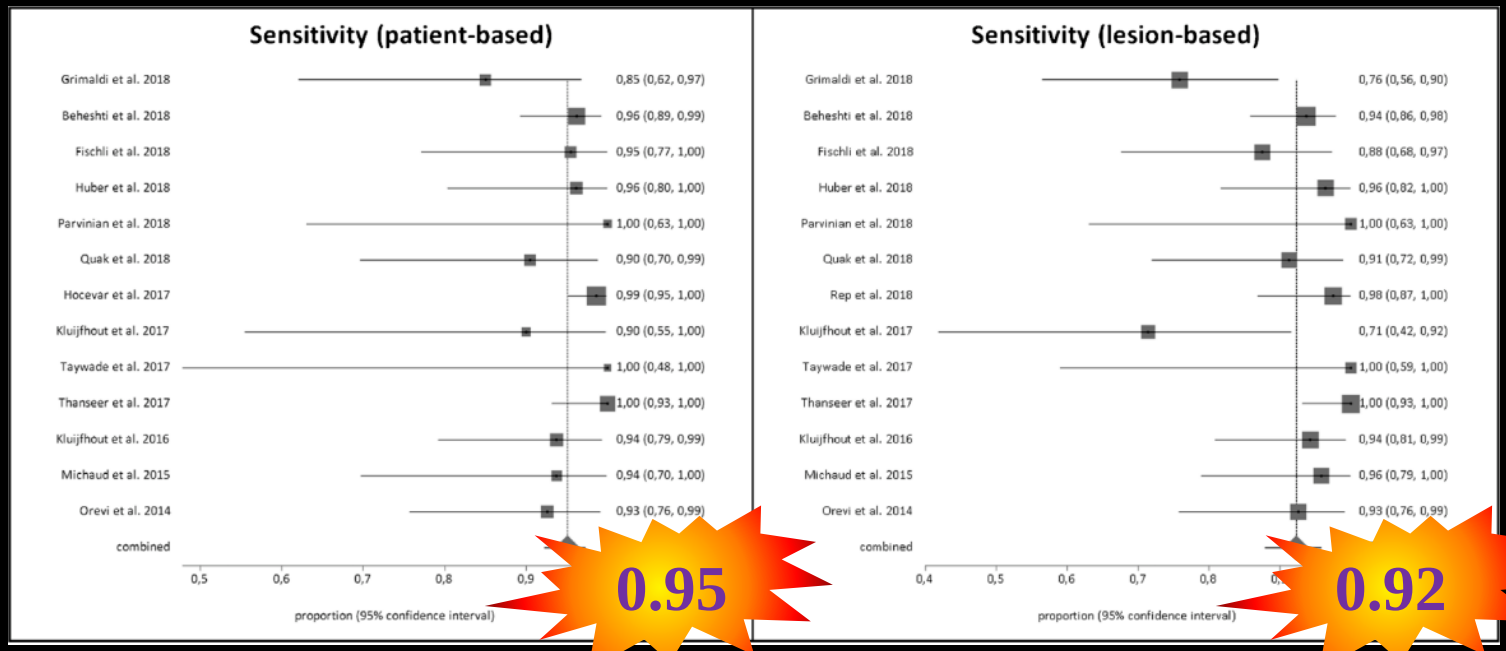
The Holy Grail of evidence

Diagnostic performance of choline PET for detection of hyperfunctioning parathyroid glands in hyperparathyroidism: a systematic review and meta-analysis

Giorgio Treglia[1,2,3,4] · Arnoldo Piccardo[1] · Alessio Imperiale[5,6] · Klaus Strobel[7] · Philipp A. Kaufmann[8] · John O. Prior[4] · Luca Giovanella[1]

Eur J Nucl Med Mol Imaging. 2019 Mar;46(3):751-765.



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- ✓ Image protocol, Refined
- Unmet needs? Have we figured all them out?
- Questions not yet addressed?

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Authors	Radiotracer	Hybrid imaging modality	Mean injected activity	Time interval between radiotracer injection and image acquisition	Image analysis
Grimaldi et al. [22]	^{18}F-choline	PET/CT (low-dose CT)	100 MBq	30 min	Visual and semi-quantitative (SUV_{max})
Beheshti et al. [23]	^{18}F-choline	PET/CT (low-dose CT in most patients)	3.2 MBq/kg	60 min and optional 100–120 min	Visual and semi-quantitative (SUV_{max})
Fischli et al. [24]	^{18}F-choline	PET/CT (contrast-enhanced CT)	160 MBq	45 min	Visual
Huber et al. [25]	^{18}F-choline	PET/CT or PET/MRI	151 MBq	NR	Visual
Parvinian et al. [26]	^{11}C-choline	PET/CT (low-dose CT)	NR	NR	Visual and semi-quantitative (SUV_{max})
Quak et al. [27]	^{18}F-choline	PET/CT (low-dose CT)	1.5 MBq/kg	60 min	Visual and semi-quantitative (SUV_{max})
Rep et al. [28]	^{18}F-choline	PET/CT (low-dose CT)	100 MBq	5 min and 60 min	Visual
Hocevar et al. [29]	^{18}F-choline	PET/CT (low-dose CT)	100 MBq	5 min and 60 min	Visual
Kluijfhout et al. [30]	^{18}F-choline	PET/MRI	188 MBq	0 (dynamic imaging for 40 min)	Visual and semi-quantitative (SUV_{max})
Taywade et al. [31]	^{18}F-choline	PET/CT (low-dose CT)	185 MBq	60 min	Visual and semi-quantitative (SUV_{max})
Thanseer et al. [32]	^{18}F-choline	PET/CT (low-dose CT)	150–185 MBq	10–15 min and 60 min	Visual and semi-quantitative (SUV_{max})
Kluijfhout et al. [33]	^{18}F-choline	PET/CT (low-dose CT)	2 MBq/kg	30 min	Visual and semi-quantitative (SUV_{max})
Kluijfhout et al. [34]	^{18}F-choline	PET/CT (low-dose CT)	2 MBq/kg	30 min	Visual and semi-quantitative (SUV_{max})
Michaud et al. [35]	^{18}F-choline	PET/CT (low-dose CT)	3 MBq/kg	0 (dynamic imaging for 10 min followed by a static acquisition)	Visual and semi-quantitative (SUV_{max})
Rep et al. [36]	^{18}F-choline	PET/CT (low-dose CT)	100 MBq	5 min, 60 min and 120 min	Visual and semi-quantitative (SUV_{max})
Lezaic et al. [37]	^{18}F-choline	PET/CT (low-dose CT)	100 MBq	5 min and 60 min	Visual
Michaud et al. [38]	^{18}F-choline	PET/CT (low-dose CT)	3 MBq/kg	0 (dynamic imaging for 10 min followed by static acquisition)	Visual
Orevi et al. [39]	^{11}C-choline	PET/CT (low-dose CT)	370 MBq	NR	Visual and semi-quantitative (SUV_{max})

Eur J Nucl Med Mol Imaging. 2019 Mar;46(3):751-765.

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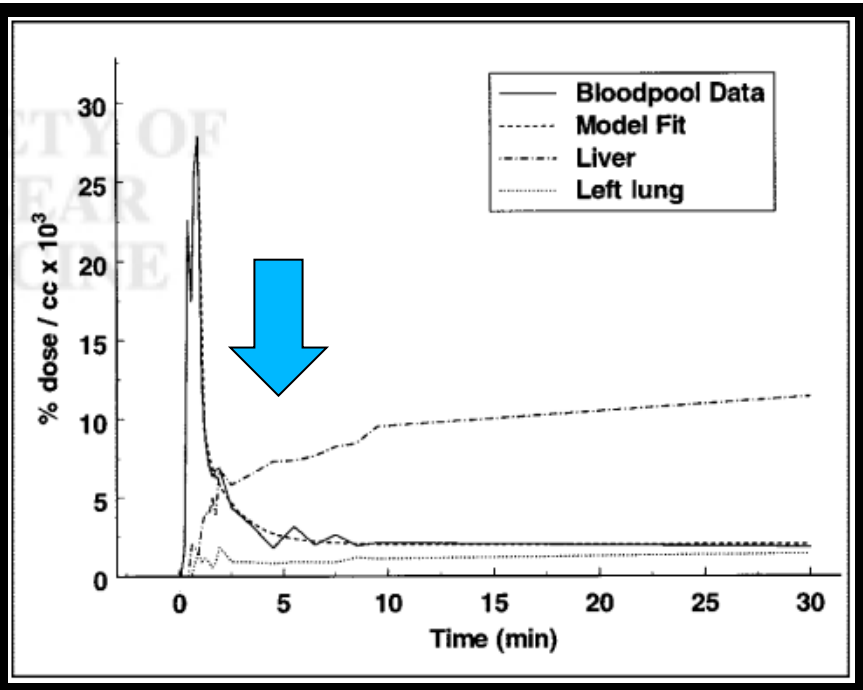
JNM The Journal of NUCLEAR MEDICINE

Pharmacokinetics and Radiation Dosimetry of ^{18}F-Fluorocholine

Timothy R. DeGrado, Robert E. Reiman, David T. Price, Shuyan Wang and R. Edward Coleman

J Nucl Med. 2002;43:92-96.



J Nucl Med. 2002 Jan;43(1):92-6.

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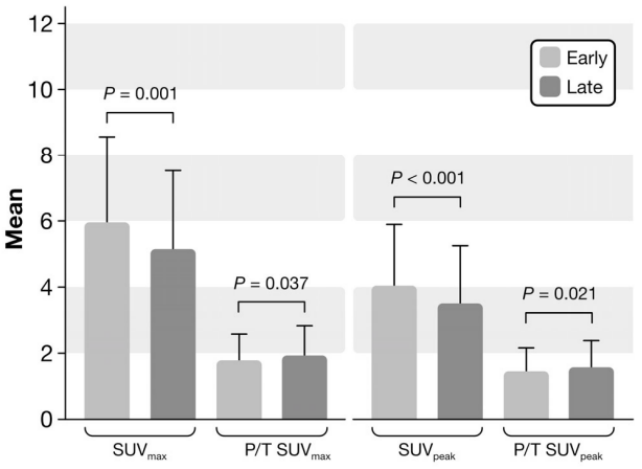
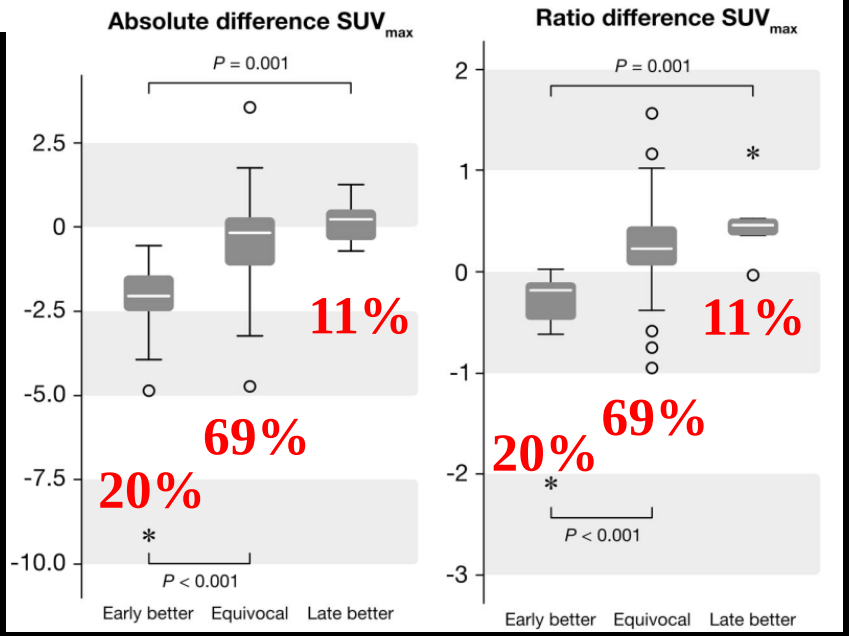
JNM The Journal of NUCLEAR MEDICINE

Dual-time-point ^{18}F-fluorocholine PET/CT in Parathyroid Imaging

Wouter Broos, Maurits Wondergem, Friso van der Zant and Remco Knol

J Nucl Med.
Published online: March 15, 2019.
Doi: 10.2967/jnumed.118.225599





J Nucl Med. doi: 10.2967/jnumed.118.225599.

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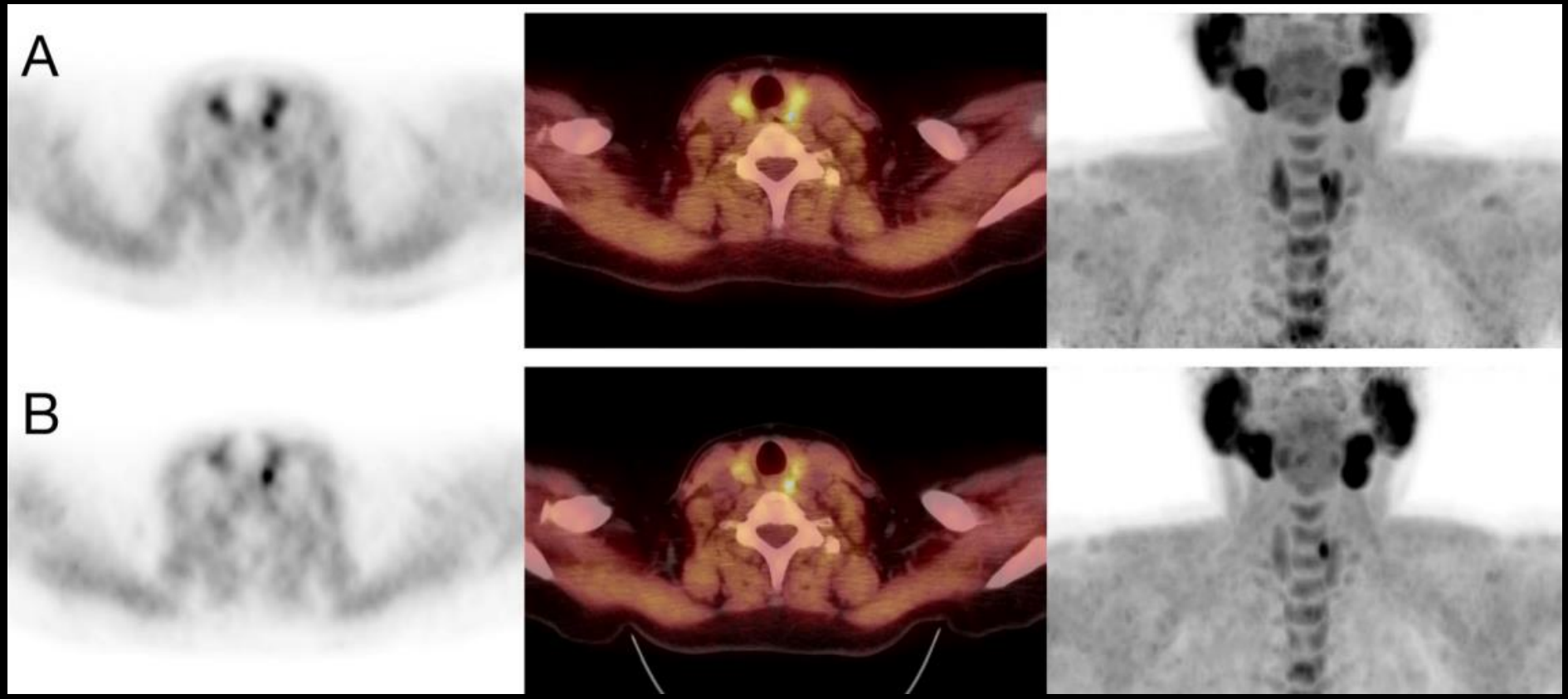

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Accuracy

The sensitivity for detection of parathyroid adenomas larger than 300 mg in size is greater than 85–90% but is less for smaller adenomas. The most common cause for a false negative study is the small size of the adenoma. The sensitivity for detection of hyperplasia is considerably lower than adenoma (~50–60%). The most common cause for a false positive study is a thyroid adenoma.

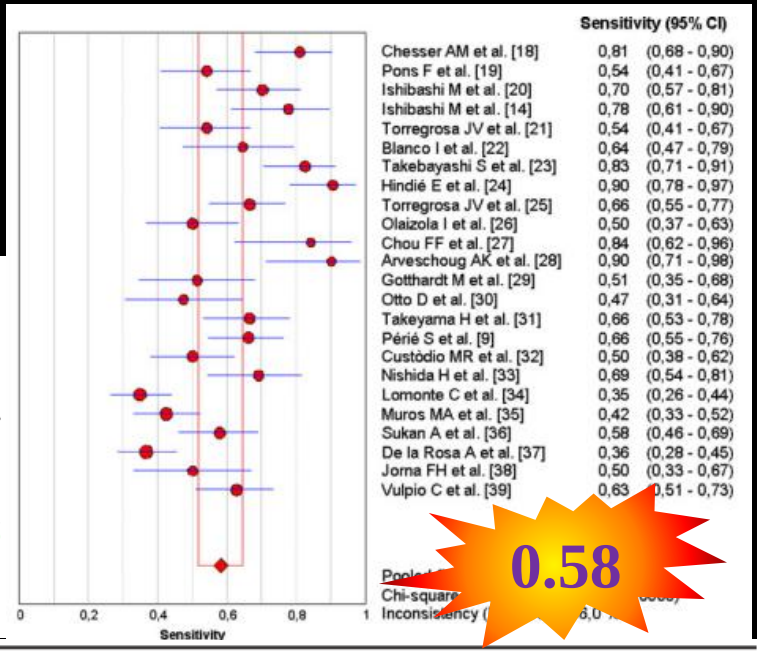

TABLE 1. Performance of Different ^{99m}Tc-MIBI Parathyroid Planar Scintigraphy Protocols in Secondary Hyperparathyroidism

	Tracers Used	Pinhole Collimator	Studies/Patients/Number of Lesions*	Sensitivity (%)*
A	^{99m}Tc-MIBI only "dual-phase"	No	15/308/899	56.2 (505/899)
B	^{99m}Tc-MIBI only "dual-phase"	Yes	4/60/196	63.2 (124/196)
C	^{99m}Tc-MIBI + ^{123}I (simultaneous acquisition plus subtraction)	Yes	2/31/126	75.4 (95/126)
D	^{99m}Tc-MIBI + $^{99m}TcO_4$ (non-simultaneous)	No	2/51/178	51.7 (92/178)
E	^{99m}Tc-MIBI + $^{99m}TcO_4$ (non-simultaneous)	Yes	1/21/78	62.8 (49/78)

Comparison between imaging protocols were performed using chi-squared test: A vs. B ($P = 0.082$); A vs. C ($P < 0.001$); B vs. C ($P = 0.031$).

*Data were extracted from Tables 1 to 3 of the paper published by Caldarella,[33] and sensitivity was calculated based on these data.

Clin Nucl Med. 2013 Aug;38(8):630-5.
Ann Nucl Med. 2012 Dec;26(10):794-803.

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Source	Patients, No.	Country	Type of Examination/Evidence	Sensitivity/NPV, %	Specificity/PPV, %	HPT			MEN I	Adenoma	Hyperplasia
						1°	2°	3°			
Lezaic et al,[13] 2014	24	Slovenia	PC/II	92/ND	100/ND	24	0	0	0	17	5
Michaud et al,[14] 2014	12	France	CS/IV	92/ND	ND/ND	8	4	0	0	7	5
Kluijfhout et al,[15] 2015	5[a]	Netherlands	ReC/III	80/ND	ND/ND	5	0	0	0	5	2
Michaud et al,[16] 2015	17	France	PC/II	94/ND	85/ND	11	6	0	3	9	5
Hocevar et al,[17] 2017	151[a]	Slovenia	ReC/III	83/ND	ND/ND	135	11	0	0	128	11
Kluijfhout et al,[18] 2016	44[a]	Netherlands	ReC/III	94/ND	ND/97	40	0	1	3	25	7
Imamovic et al,[19] 2016	34[a]	Austria	PC/II	97/ND	ND/ND	34	0	0	0	33	0
Quak et al,[20] 2018	25[a]	France	PC/II	90/ND	ND/87	23	0	0	0	22	1
Huber et al,[21] 2018	26	Switzerland	ReC/III	96/ND	ND/100	24	1	0	1	24	1
Thanseer et al,[22] 2017	54	India	PC/II	100/ND	96/ND	54	0	0	0	54	0
Rep et al,[23] 2018	36	Slovenia	PC/II	97/ND	95/ND	36	0	0	0	33	1
Grimaldi et al,[24] 2018	27[a]	France	PC/II	81/86	ND/94	27	0	0	0	14	11
Araz et al,[25] 2018	35	Turkey	PC/II	96/93	100/ND	35	0	0	0	0	0
Bossert et al,[26] 2018	34[a]	Italy	PC/II	88/ND	100/ND	34	0	0	0	17	0
Beheshti et al,[27] 2018	82[a]	Austria	PC/II	93/97	96/90	76	0	0	0	60	7
Zajícová et al,[28] 2018	13[a]	Czech Republic	ReC/III	92/100	ND/ND	13	0	0	0	11	3

JAMA Otolaryngol Head Neck Surg. doi: 10.1001/jamaoto.2019.0574.

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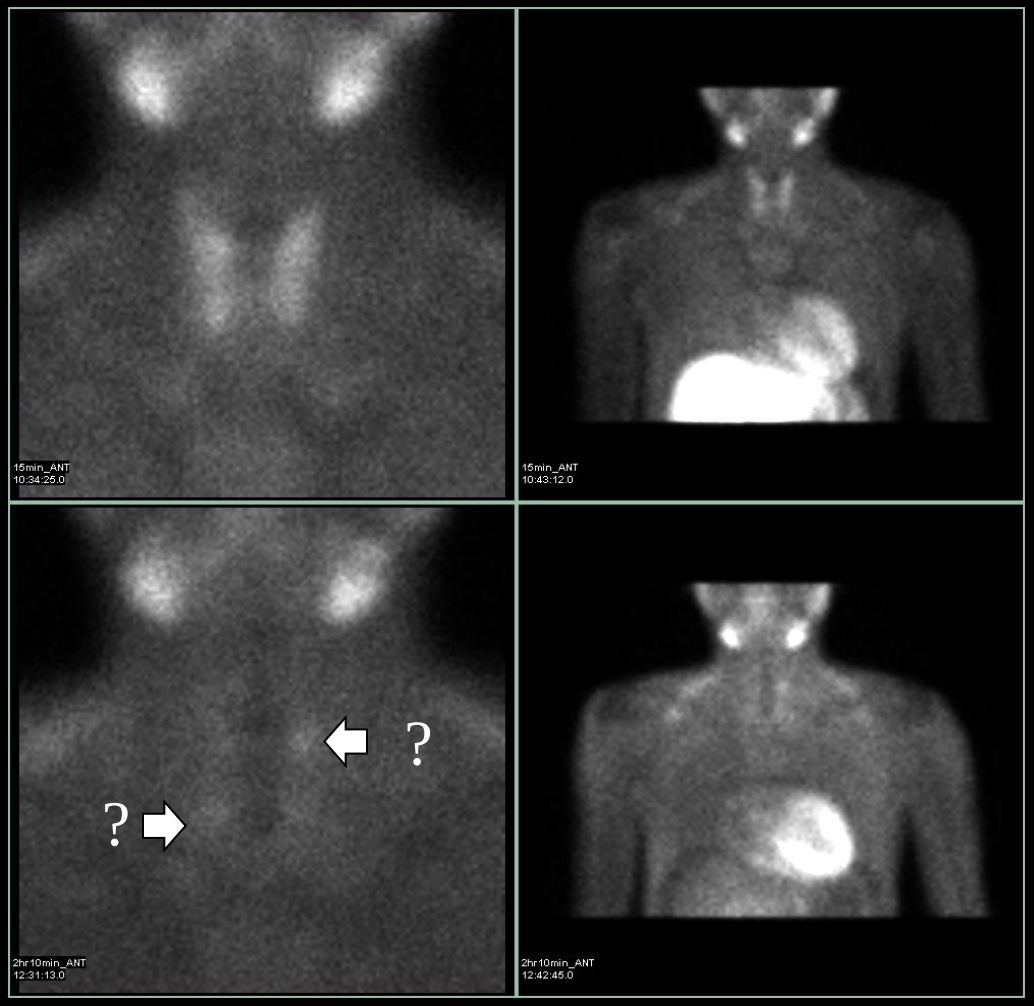
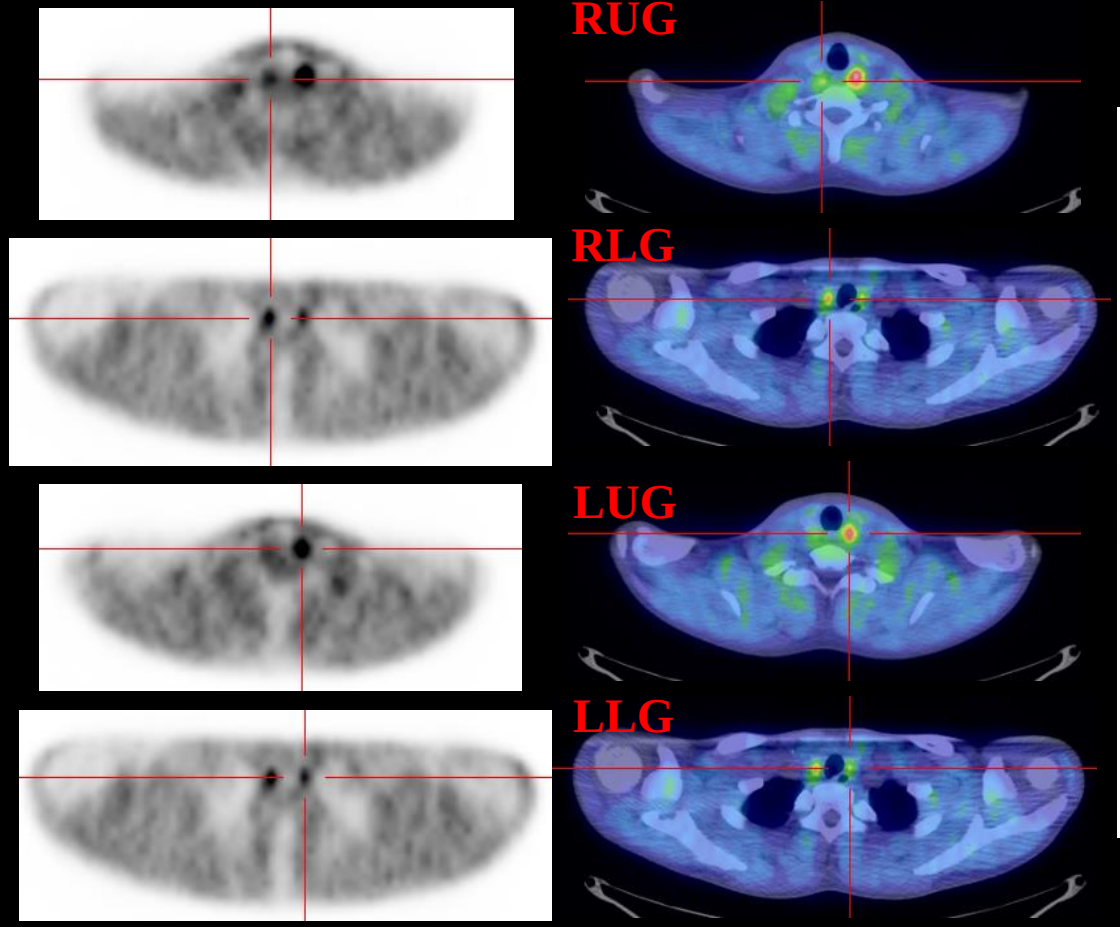


iPTH = 2281.4 pg/mL

Data not yet published



iPTH = 2281.4 pg/mL

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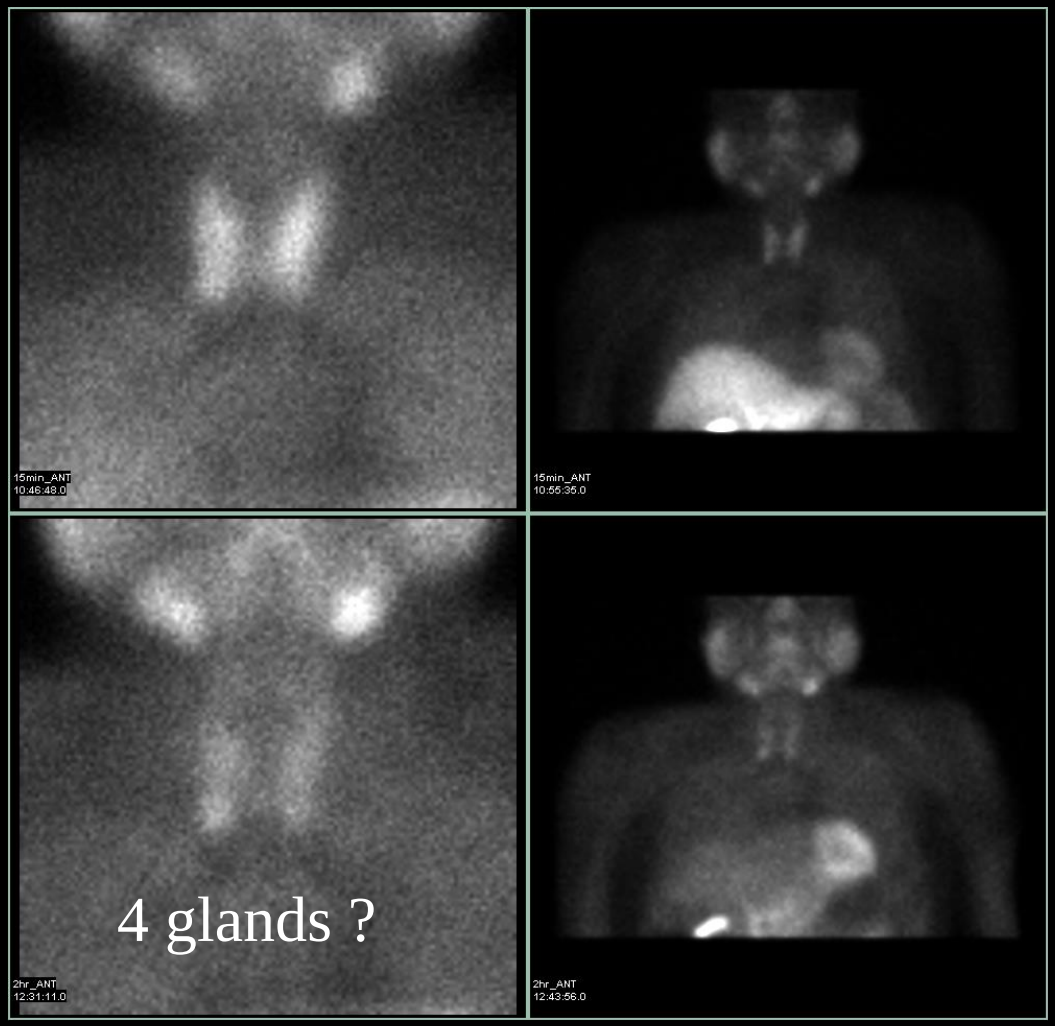
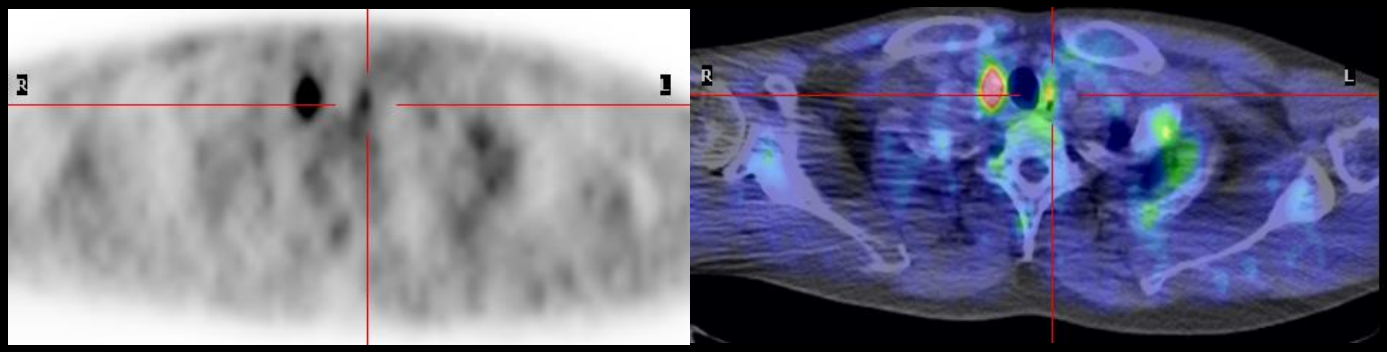


iPTH = 1844.8 pg/mL

Data not yet published

RLG & LLG

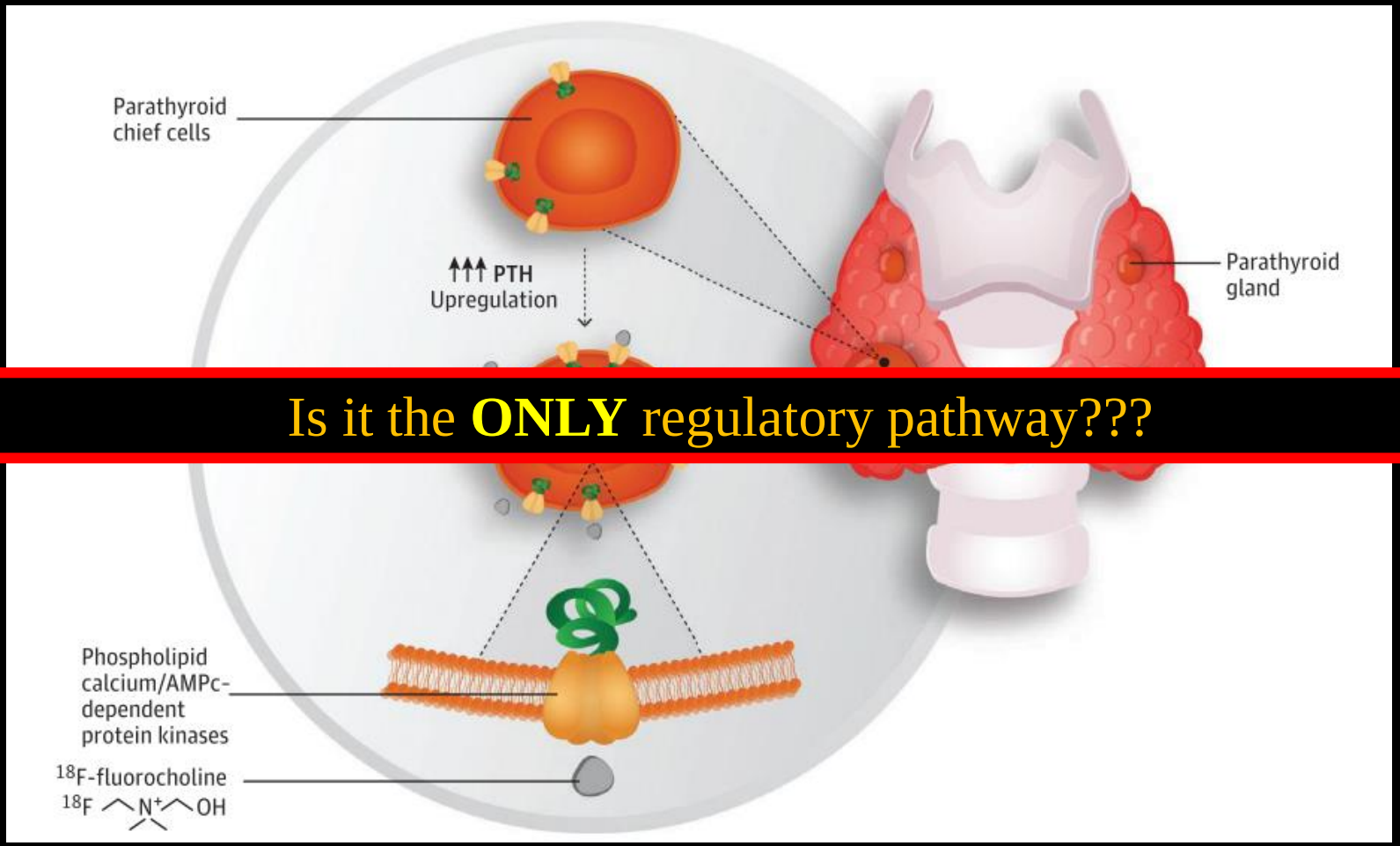


RLG (450 mg) & LLG (360 mg) total parathyroidectomy

iPTH = 1844.8 => 375 pg/mL

Data not yet published

Why does it work better?



Is it the **ONLY** regulatory pathway???

JAMA Otolaryngol Head Neck Surg. doi: 10.1001/jamaoto.2019.0574.

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Other Considerations

- Parathyroidectomy for secondary/tertiary hyper-PTH
  - Pre-operative imaging required for every patients???
  - Sensitivity in patients before Re-operation
  - Real world clinical application? (Marketing)

Conclusion

- Choline PET & hyperparathyroidism
  - Science: Choline PET better than traditional images (primary)
  - Choline PET in secondary hyperparathyroidism ?
  - Study of mechanism
  - Real world clinical application and Marketing

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Acknowledgement

- Department of Surgery, Hualien Tzu-Chi General Hospital
  - Hwa-Tsung Chen
  - Ming-Che Lee
- Department of Nuclear Medicine, Hualien Tzu-Chi General Hospital
- Department of Nuclear Medicine, Chung Shan Medical University Hospital
  - Pan-Fu Kao
- Society of Nuclear medicine, Taiwan

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Thank you!!!

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