

**THREE-QUANTA
POSITRON ANNIHILATION
IN BLOOD SAMPLES OF
DIFFERENT OXYGENATION LEVELS**

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THREE-QUANTA POSITRON ANNIHILATION

1. WHY

2. CONTROVERSIES

3. HOW

THREE-QUANTA POSITRON ANNIHILATION

Used in material science but not
medical imaging

Positron Emission Tomography
(PET) currently is based on
TWO-QUANTA annihilations
only



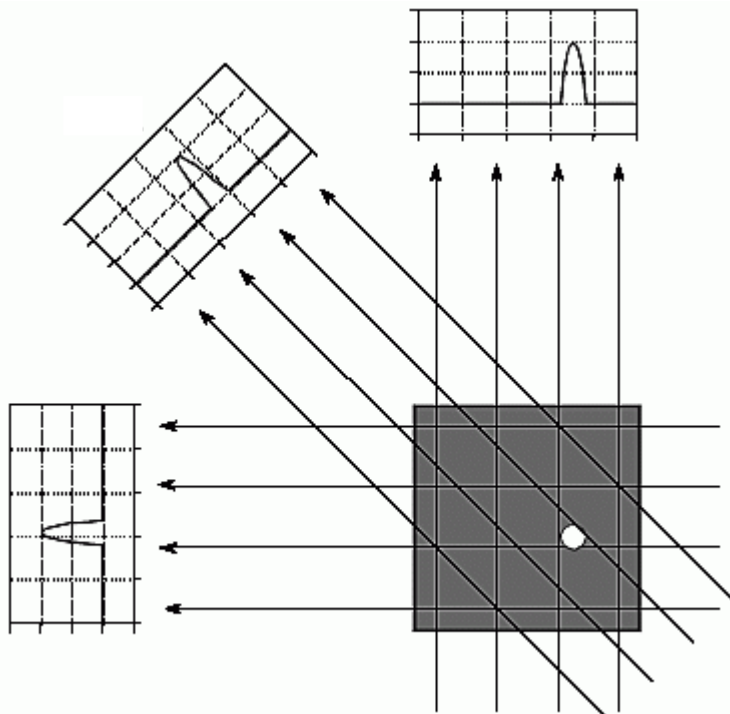
THREE-QUANTA POSITRON ANNIHILATION

Attractions:

1. Image reconstruction without backprojection
2. Molecular imaging without dedicated radiopharmaceutical or contrast agent

2 γ PET

IMAGE RECONSTRUCTION



WE HAVE TO BACK-PROJECT
COZ WE DON'T KNOW AT WHICH
POINT THE ANNIHILATION
HAPPENED

LINE OF RESPONSE

3 γ PET

By conservations of
energy & momentum

KNOWN

(E_1, α_1)

(E_2, α_2)

(E_3, α_3)

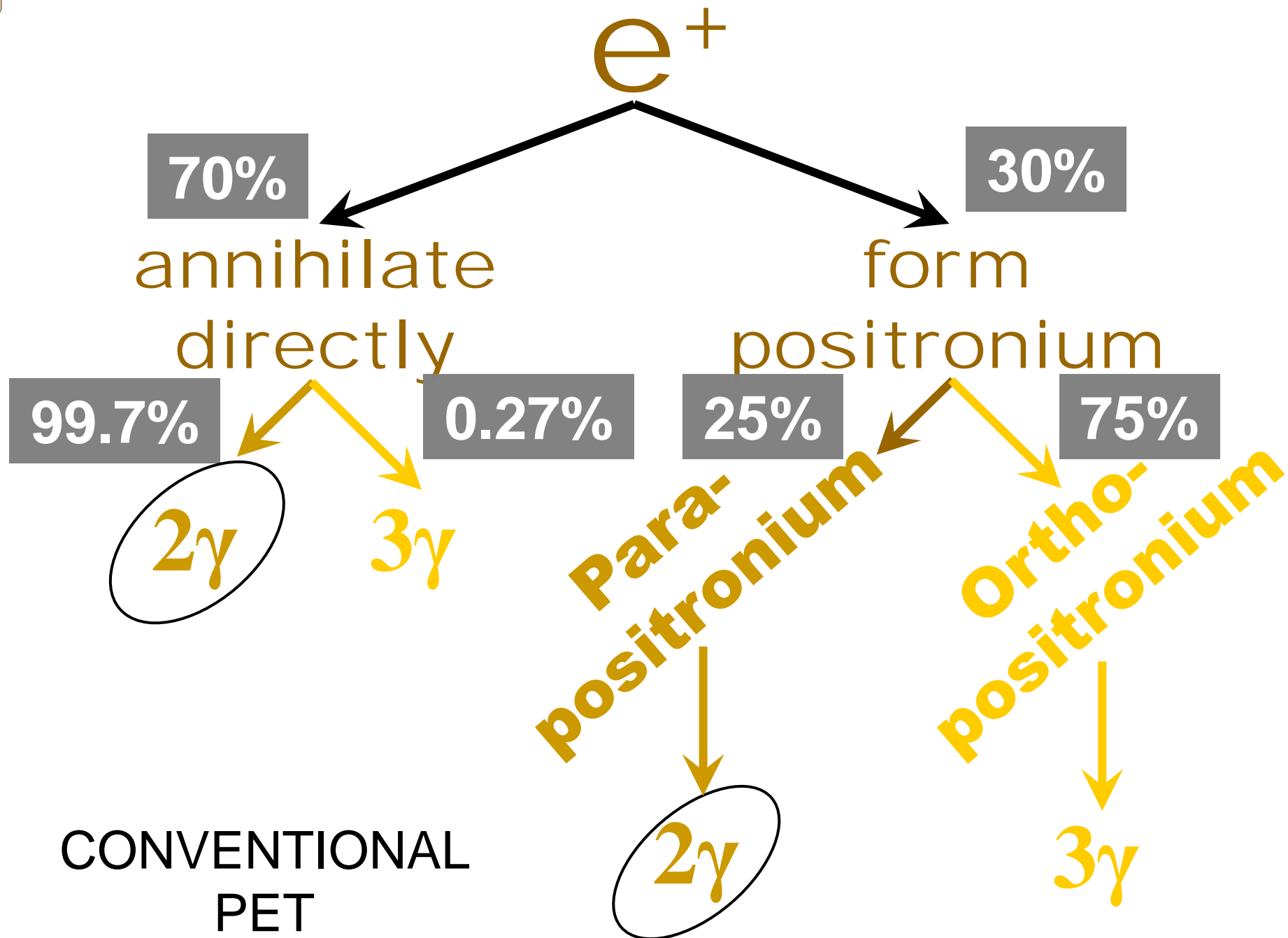
UNKNOWNNS

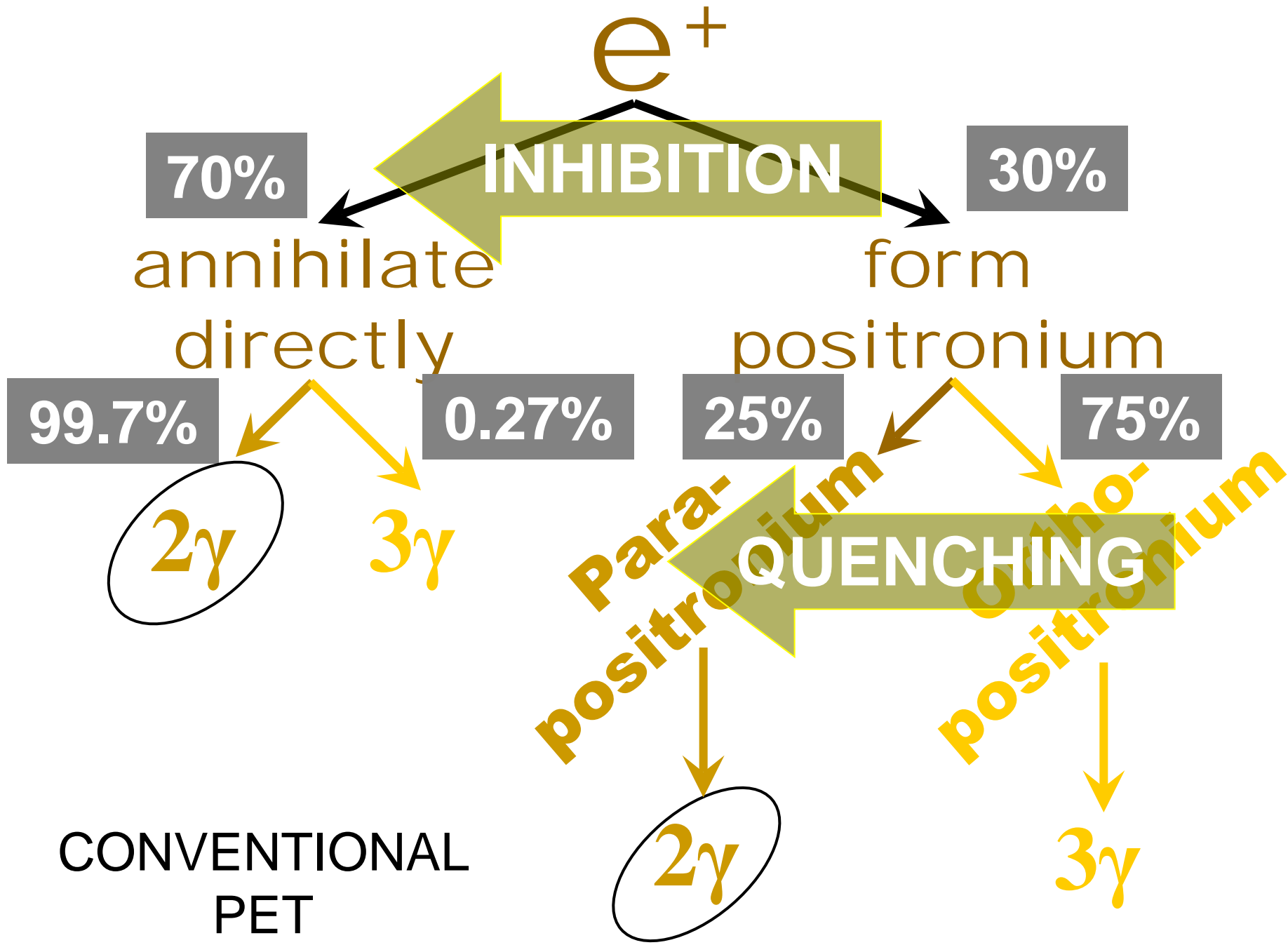
(x_1, y_1, z_1)



solve simultaneous eqs

POINT OF RESPONSE







INHIBITION

annihilate
directly

form
positronium

AGENTS eg
 O_2 , NO, CO_2

oxygenation

**Para-
positronium**

QUENCHING

**Ortho-
positronium**

PROSPECTS FOR MOLECULAR IMAGING



MEASURE $3\gamma/2\gamma$ YIELD



FIND OUT O_2 IN BODY TISSUES?

**PROSPECTS FOR
MOLECULAR IMAGING**

PROPOSAL

**Three-Gamma Annihilation Imaging in Positron
Emission Tomography**

Krzysztof Kacperski*, Nicholas M. Spyrou, and F. Alan Smith

Abstract—It is argued that positron annihilation into three photons, although quite rare, could still be used as a new imaging modality of positron emission tomography. The information gained when the three decay photons are detected is significantly higher than in the case of 511 keV two-gamma annihilation. The performance of three-gamma imaging in terms of the required detector properties, spatial resolution and counting rates is discussed. A simple proof-of-principle experiment confirms the feasibility of the new imaging method.

Index Terms—Positron emission tomography, three-gamma annihilation.

Three-gamma imaging is potentially more powerful than standard PET because each event bears the complete position information enabling the localization of the activity distribution without use of back-projection tomographic techniques. However, only a subfraction of the three-photon events are usable as each photon energy must be above the detection threshold and only total energy deposition events can be used, as a tight total energy window and time window (<5 ns) must be applied (for typical source strengths used in imaging) to reduce the strong background from two-photon decay pile-up events. However, these conditions can be met with high-resolution semiconductor detectors as pointed out in Kacperski and Spyrou (2005), and construction of a detection system with the required attributes for such studies is not beyond the reach of current technology.

The present work answers one question raised by Kacperski and Spyrou (2005) concerning the potential biological sensitivity of the three-photon imaging. Unfortunately, one should not expect any sensitivity to the level of dissolved O_2 . Our results indicate that the overall three-photon yield is about 0.5% in all samples. These conclusions assume that the direct three-photon yield is identical to that for free e^- s. Only direct measurement of the three-photon yield can determine if this assumption is correct (Seweryniak 2006).



Table 1. The delayed (F_3^{de}) and total (F_3) three-photon yields as well as the fit parameters (K_p and K_{cap}/λ_d) for the various liquid samples (HSA is for human serum albumin).

Material	Oxygen	F_3^{de} (%)	F_3 (%)	K_p (ns ⁻¹)	$R = K_{\text{cap}}/\lambda_d$
Iso-octane	Low	0.58	0.85	1.34	2.15
	High	0.39	0.65	2.27	2.06
Water	Low	0.26	0.52	2.77	3.05
	High	0.25	0.51	2.84	3.07
Saline	Low	0.24	0.51	2.86	3.14
	High	0.24	0.51	2.98	3.07
HSA	Low	0.25	0.51	2.64	3.30
	High	0.25	0.51	2.95	2.96
Blood	Venous	0.25	0.52	2.86	3.02

The present work answers one question raised by Kacperski and Spyrou (2005) concerning the potential biological sensitivity of the three-photon imaging. Unfortunately, one should not expect any sensitivity to the level of dissolved O₂. Our results indicate that the overall three-photon yield is about 0.5% in all samples. These conclusions assume that the direct three-photon yield is identical to that for free e⁻s. Only direct measurement of the three-photon yield can determine if this assumption is correct (Seweryniak 2006).

DATA TO BE PRESENTED HERE

The GAMMASPHERE detector system when it was stationed at Argonne National Laboratory

4π array of 110 Compton-suppressed high-purity germanium detectors (HPGe)

Experiment carried out by Dr K Kacperski when he was employed as a postdoc at the University of Surrey



source: www.nuclear.kth.se

GAMMASPHERE: AN UNPRECEDENTED LUXURY FOR US

LUXURY #1 NEAR-4 π SOLID ANGLE

LUXURY #2 MULTI-DIMENSIONAL DATA WRITTEN OUT

GAMMASPHERE information, EVENT DATA RECORD

The EVENT DATA RECORD consists of a header and data as:

```
typedef struct event_buffer
{
    u_short RecordType;          /* 0 event data type= 3          */
    u_short RecordLength;       /* 1 number of bytes in this record */
    u_short RecordVer;         /* 2 record version or subtype    */
    u_short HeaderBytes;       /* 3 number of bytes in header    */
    u_short EffNumber;         /* 4 eff processor number         */
    u_short StreamID;          /* 5 event stream ID              */
    u_short EffSequence;       /* 6 eff sequence number          */
    u_short ModeFlags;          /* 7 event format flags           */
    u_short DataLength;        /* 8 number of i*2 data words     */
    u_short ChecksumType;      /* 9 type of checksum             */
    u_short Checksum;          /* 10 checksum value              */
    u_short EventData[EB_SIZE]; /* event data area                */
}
    EVENT_BUFFER;
```

GAMMASPHERE: AN UNPRECEDENTED LUXURY FOR US

LUXURY #1 NEAR-4 π SOLID ANGLE

LUXURY #2 MULTI-DIMENSIONAL DATA WRITTEN OUT

GAMMASPHERE: A MULTI-DIMENSIONAL EVENT

DATA

1	gcmode	gain correction on/off
2	tmmode	time veto on/off
3	hmode	adjacent detector veto on/off

The **EVENT** BIT - EVENT DATA CONTROL BITS FOR EACH DETECTOR

```
typedef struct {
    u_s 4 writeget      output ge time on/off
    u_s 5 writegef      output full ge data on/off
    u_s 6 writebgo      output of BGO data on/off
    u_s BIT - EVENT DATA CONROL BITS FOR EACH EVENT
    u_s
    u_s 7 writeallge    output of dirty ge data on/off
    u_s 8 writeallbgo  output of clean bgo data on/off
    u_s
    u_s BIT - MISC
    u_s
    u_s 9 writeIsomerTag
    u_s 10 rf_timing    ge times calculated vs rf pulses
    u_s                  (subtract tac2 on the fly)
} EVENT_BUFFER;
```

GAMMASPHERE: AN UNPRECEDENTED LUXURY FOR US

LUXURY #1 NEAR- 4π SOLID ANGLE

LUXURY #2 MULTI-DIMENSIONAL DATA WRITTEN OUT

GAMMASPHERE: AN UNPRECEDENTED LUXURY FOR US

LUXURY #1 NEAR-4 π SOLID ANGLE

1	hpid	bgo hit pattern	(0xfe00)	1111 1110 0000 0000	[1]
		and ge hit bit	(0x0100)	0000 0001 0000 0000	
		and id register	(0x00ff)	0000 0000 1111 1111	
2	ge_high	14 bit high res ge	(0x3fff)	0011 1111 1111 1111	
		and over-range bit	(0x4000)	0100 0000 0000 0000	
		and Pileup bit	(0x8000)	1000 0000 0000 0000	
3	ge_side	12 bit side ch ge	(0x0fff)	0000 1111 1111 1111	[2]

The appropriate mask to extract the information is shown both in hex and binary formats.

The rest of the events depend on what EFF write out options are on:

If the "writeget" [4] (germanium time) or "writegef" [5] (trap + lowres signals) are set

4	ge_time	12/13 bit[5]	ge time	(0x1fff)	0001 1111 1111 1111
---	---------	--------------	---------	----------	---------------------

If "writegef" [5] (trap + lowres signals) is set:

5	ge_trap	12 bit trap corr	(0x0fff)	0000 1111 1111 1111
6	ge_low	12 bit low res ge	(0x0fff)	0000 1111 1111 1111

If "writebgo" [6] (clean bgo) is set:

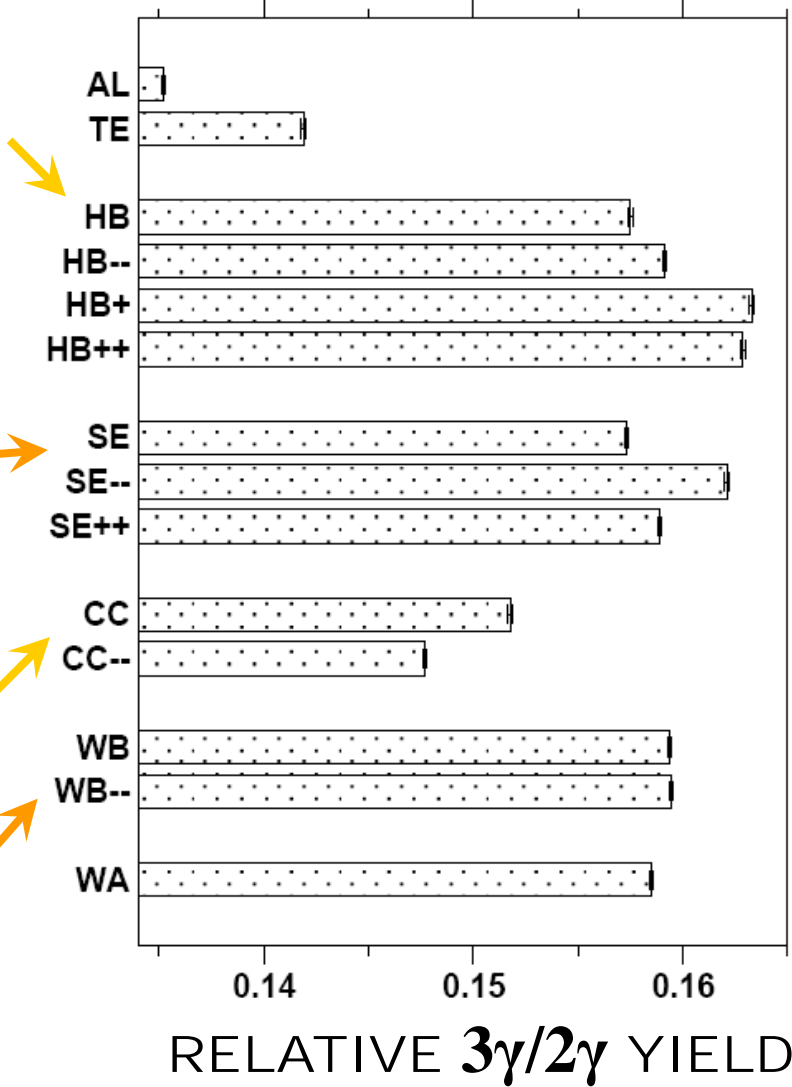
7	bgo_time	12 bit bgo time	(0x0fff)	0000 1111 1111 1111	[3]
8	bgo_low	12 bit bgo energy	(0x0fff)	0000 1111 1111 1111	[3]

HAEMOLYSED BBLOOD
(HAEMOGLOBINS HAVE
BEEN LIBERATED FROM
RED BLOOD CELLS)

SERUM
(LIKE PLASMA BUT NO
CLOTTING FACTORS)

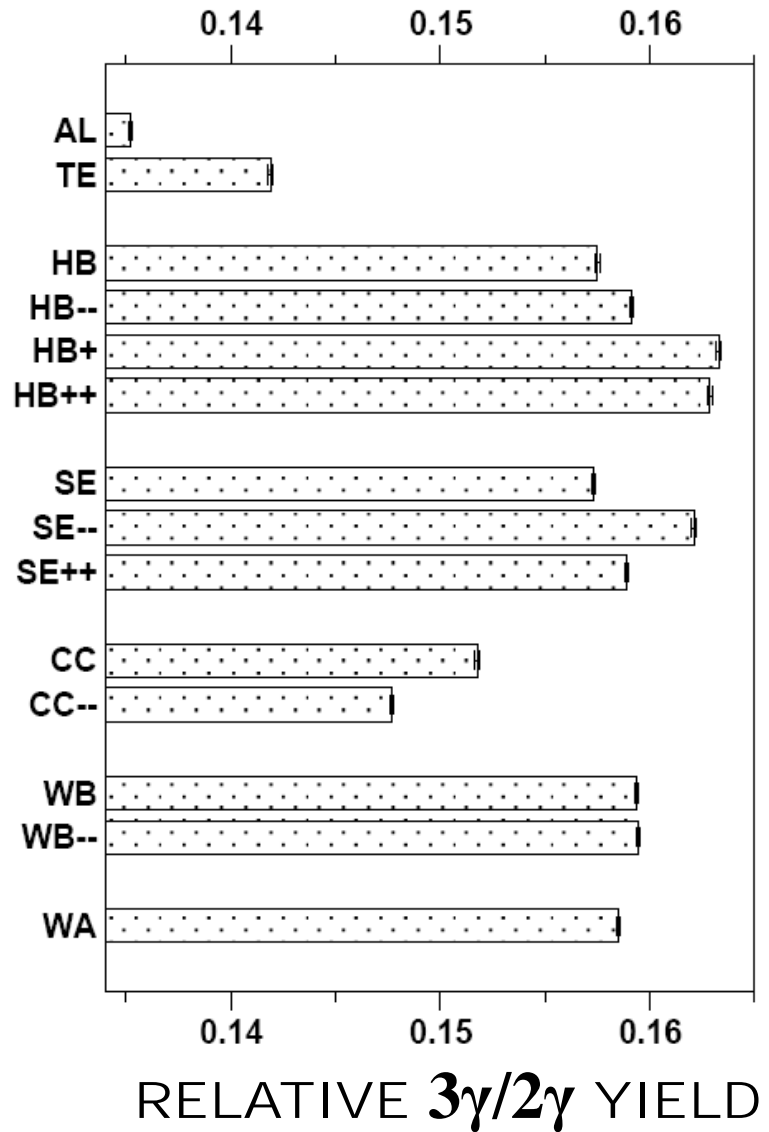
CELL CONCENTRATE
(NO PLASMA)

WHOLE BBLOOD



THE FACT THAT
THEY VARY IS
ENCOURAGING –
AT LEAST
THE METHOD IS
SENSITIVE TO
SOMETHING

OXYGENATION IS NOT
THE ONLY FACTOR.
THERE ARE
COMFOUNDING
FACTORS PERTURBING
THE 3-QUANTA YIELD



THREE-QUANTAS STUDIES: DIFFICULTIES & CHALLENGES

1. PHYSICAL MEASUREMENT

- RARE EVENTS NOT EASY TO DETECT
- DIFFICULT TO PICK OUT FROM COMPTON-SCATTERED BACKGROUND (even with Compton-suppression)
- DEAD TIME

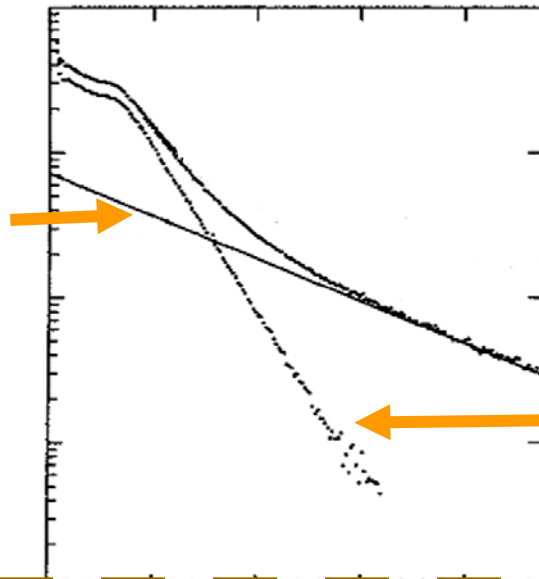
2. MONTE CARLO

- INTERACTION
- CROSS-SECTIONS
- CHEMICAL BINDING (same elemental composition bound/structured differently causes different 3-quanta yields
– *THE SAME PROPERTY WHICH LENDS THE METHOD MOLECULAR IMAGING PROSPECTS*)

DETECTION OF $3\gamma/2\gamma$ YIELDS

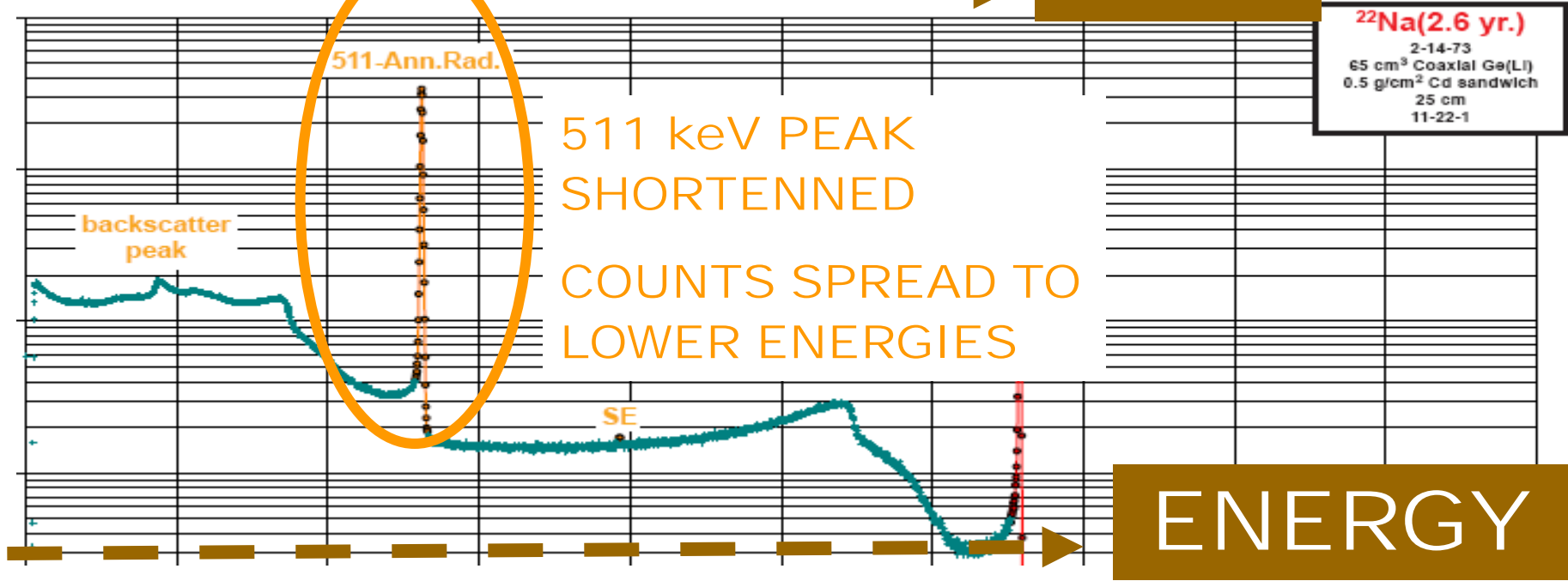
BESIDES TRIPLE
COINCIDENCE

SLOW COMPONENT
ORTHO-POSITRONIUMS
(3γ)



FAST COMPONENT
FREE POSITRONS

TIME



Characteristic x-rays from bismuth

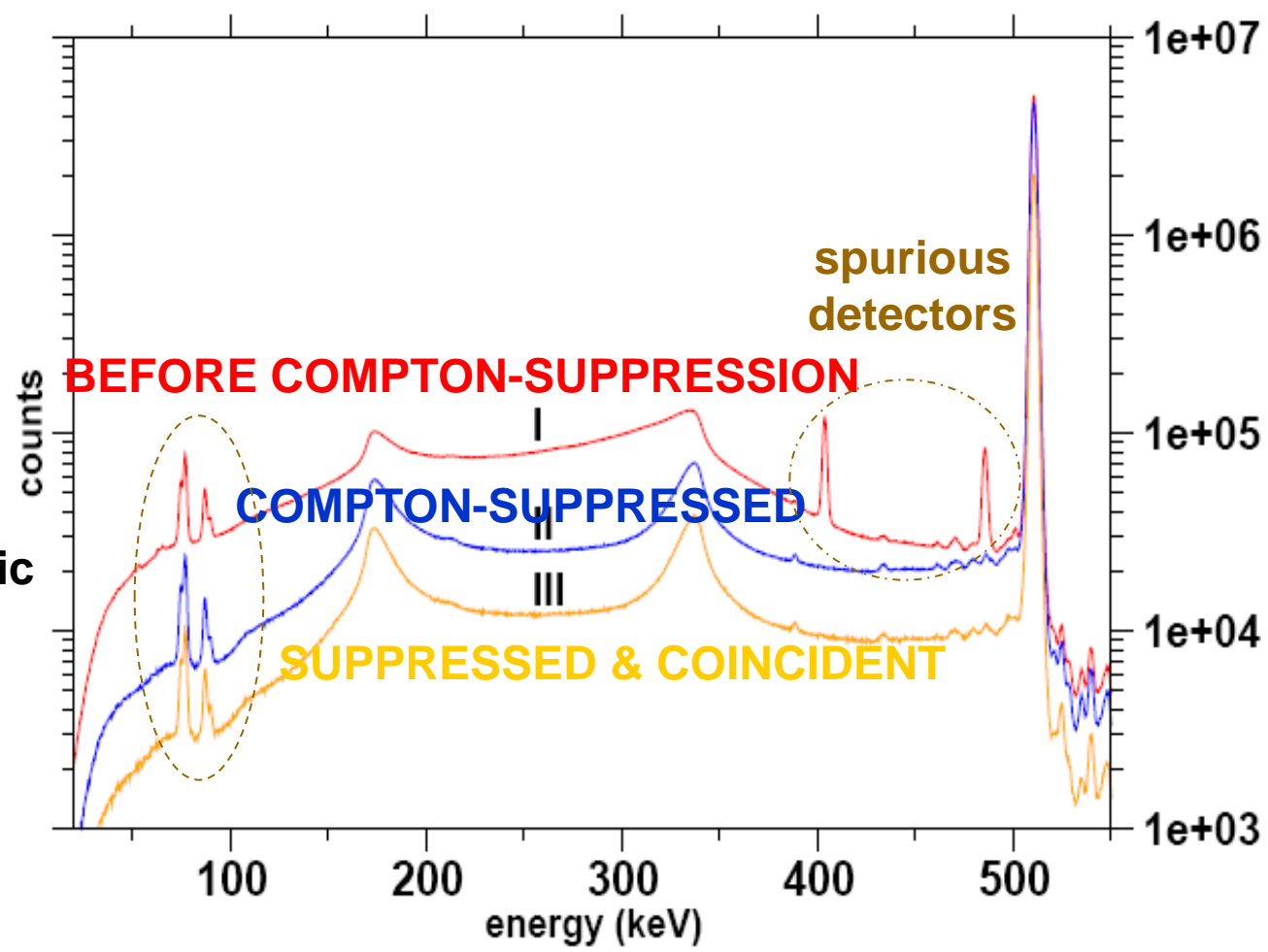
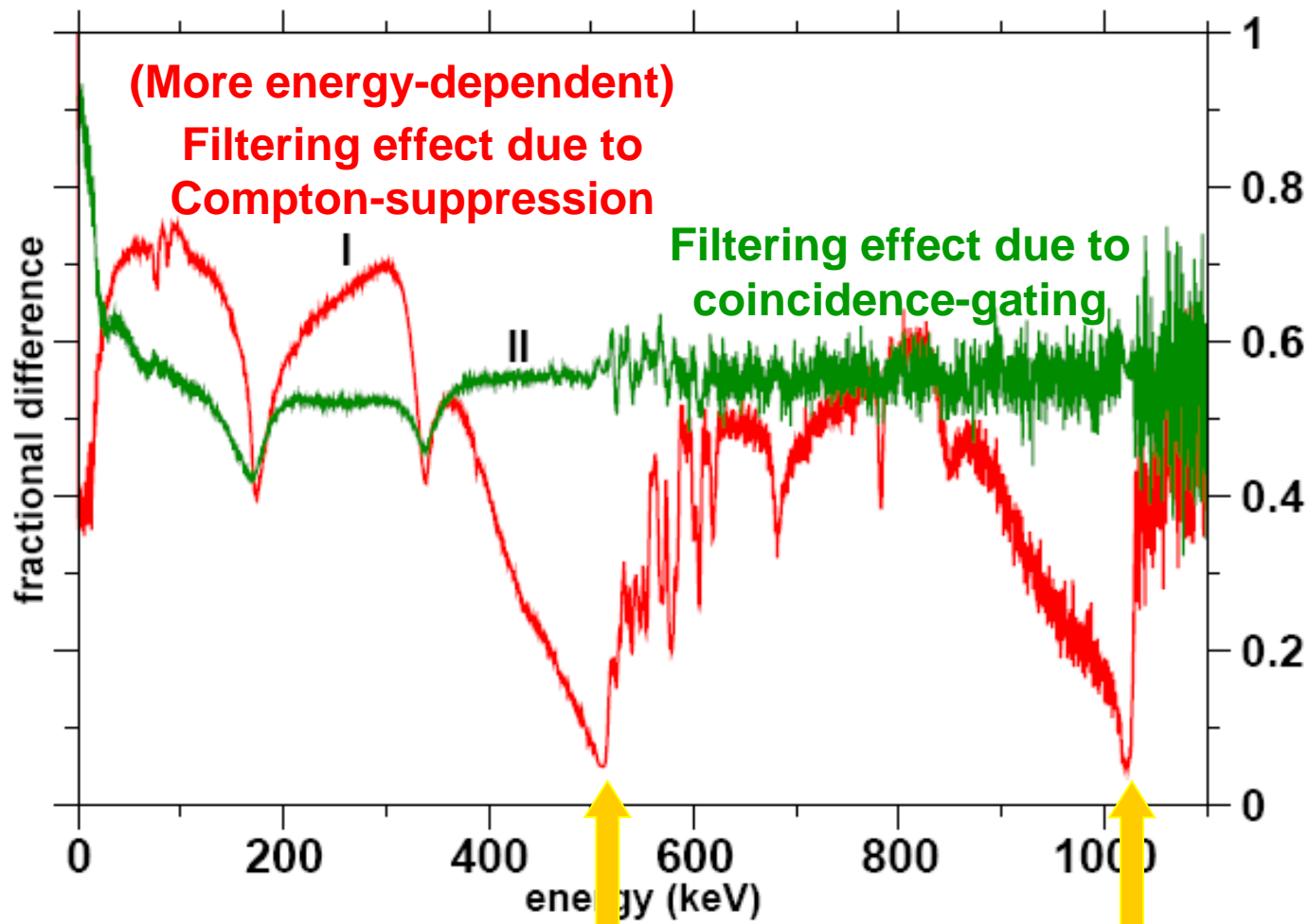


Fig. 1. Gamma spectra from the FDG source with the reference sample in place: (I) all hits from all detectors; (II) clean hits from non-outlying detectors only; (III) time-gated clean hits from non-outlying detectors only. The energy axis has been truncated.



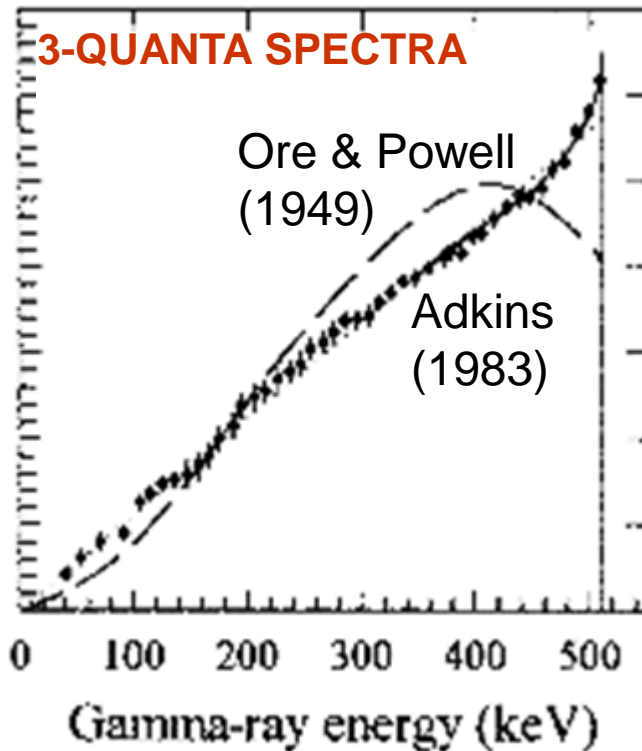
FILTERED THE LEAST: FULL-ENERGY PHOTO-PEAK & SUMMED PEAK

Fig. 2. Variation in filtering effects with energy: fractional difference in counts per energy bin (I) with and without Compton-suppression; (II) before and after time-gating.

DIFFICULTIES & CHALLENGES

STAGES OF FILTERING

1. COMPTON-SUPPRESSION
2. COINCIDENT TIME GATING
3. ANGULAR CORRELATION
4. ENERGY & MOMENTUM CONSERVATION



**IN OUR ATTEMPT TO CLEAN-UP
THE SPECTRA TO SINGLE-OUT
THREE-QUANTA COUNTS, WE
INEVITABLY REMOVE THE
COUNTS WE WANT, AND OBTAIN
THE COUNTS WE DO NOT WANT**

FURTHER WORK

TO SUPPRESS OR NOT TO SUPPRESS

FROM COMPTON-SUPPRESSION TO GAMMA-TRACKING

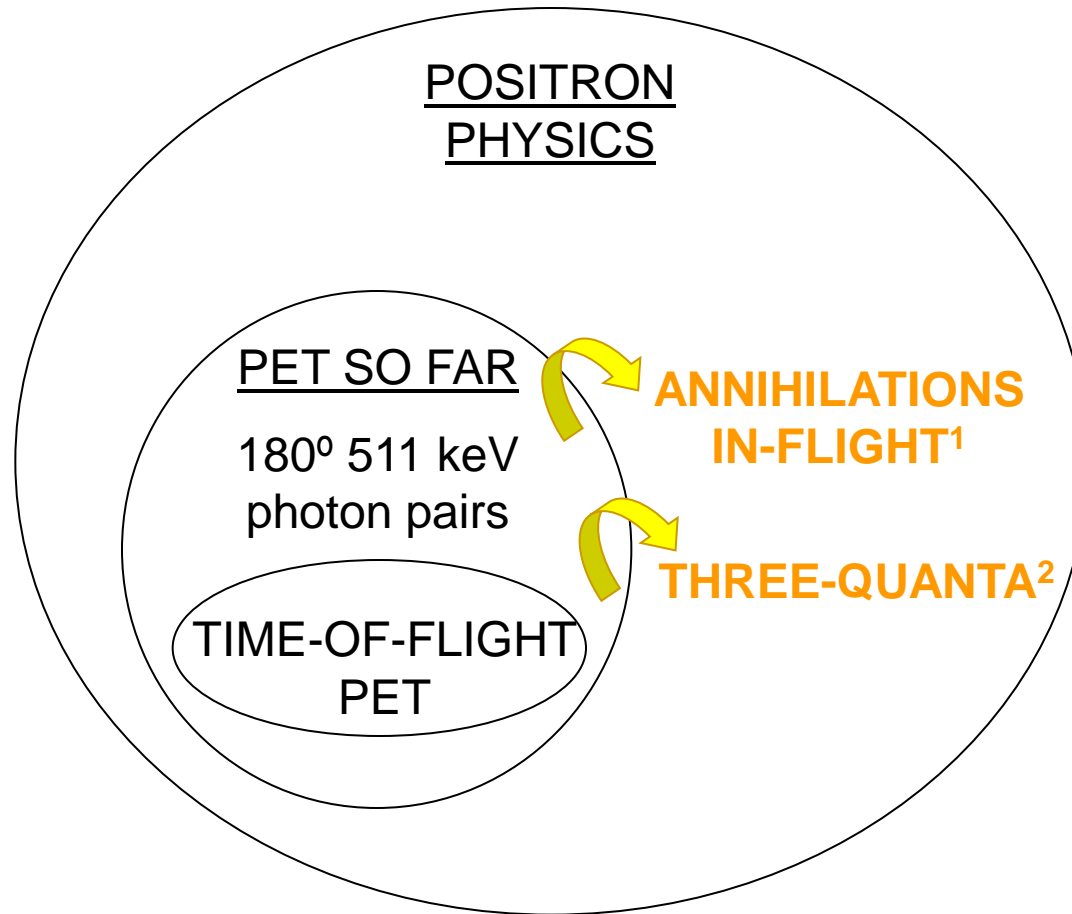
To include Compton-scattered counts instead of removing them

*Next-generation large-array detectors
(AGATA and GRETA)*

Great idea but is it going to work?

POSITRON EMISSION TOMOGRAPHY

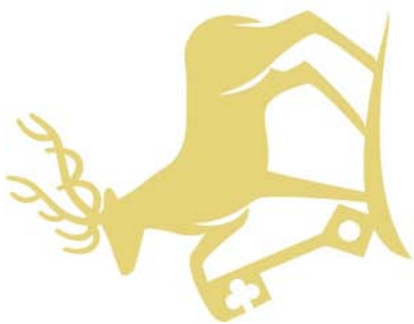
NEEDS A RETHINK



Surrey's attempts in stepping out of the 'comfort zone':

¹ Chin & Spyrou 2007 NIM-A 580:481

² Latest work: this and Alkhorayef's presented in Cancun and Lisbon



Positron about to decay in flight	1	0.606	1	2	0.155,0.023,500.314	-0.122,-0.592, 0.797
Resulting photons	1	0.979	0	2	0.155,0.023 500.314	-0.311, 0.020, 0.950
	2	0.649	0	2	0.155,0.023 500.314	0.282,-0.935,-0.213

NOT 0.511 NOT BACK-TO-BACK!

