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

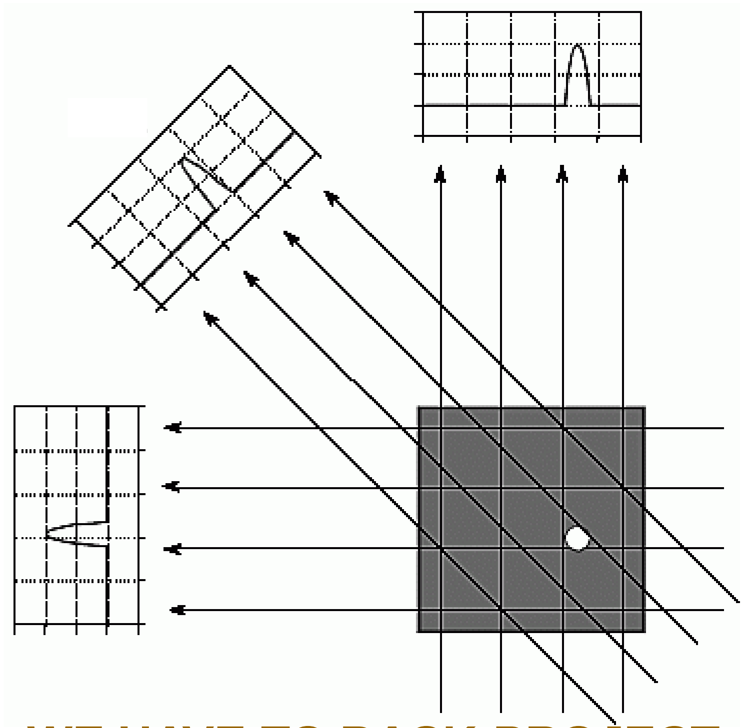
Attractions:

1. Image reconstruction without backprojection

2. Molecular imaging without dedicated radiopharmaceutical or contrast agent

2γ PET

IMAGE RECONSTRUCTION



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

LINE OF RESPONSE

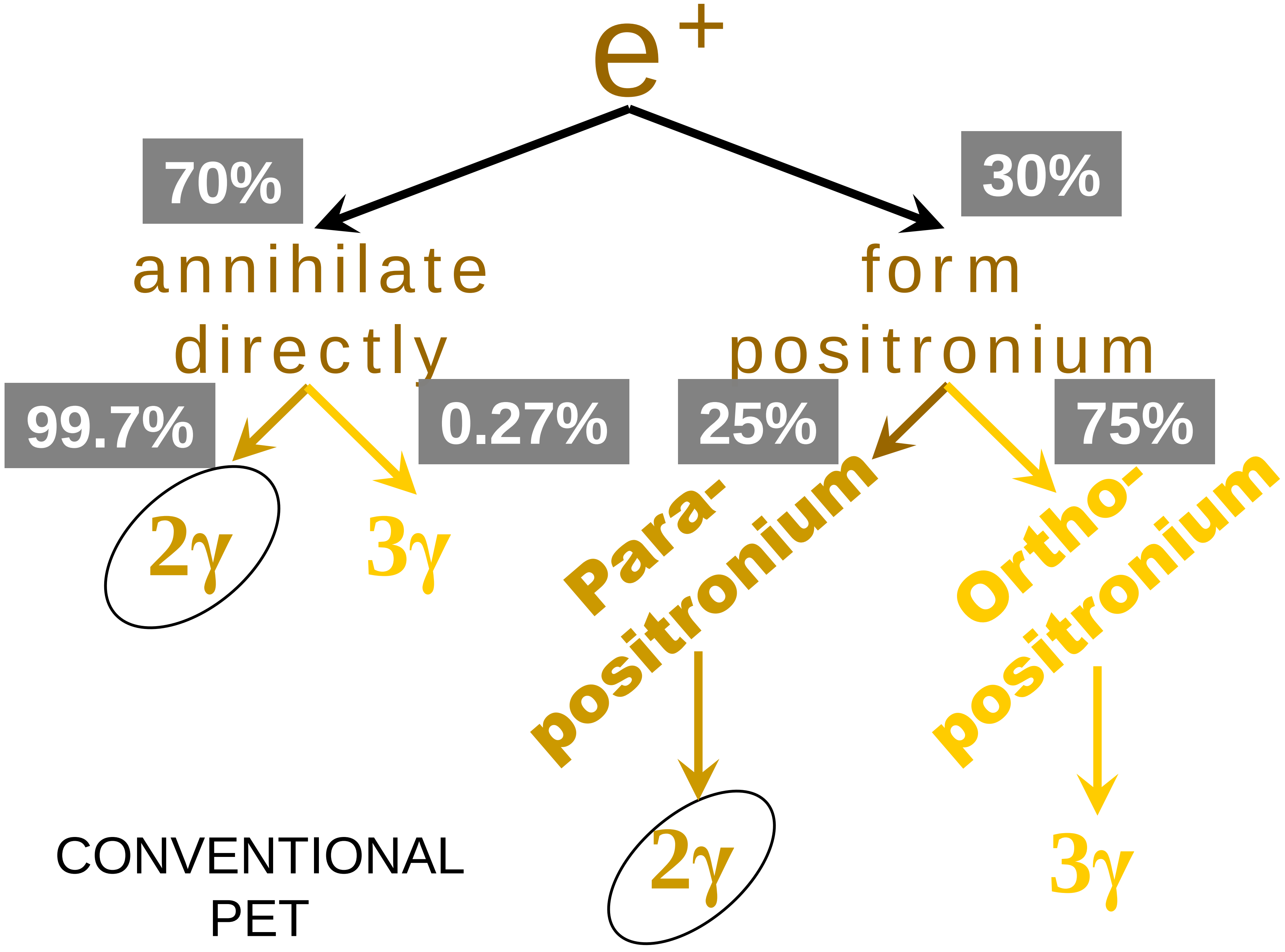
3γ PET

By conservations of energy & momentum

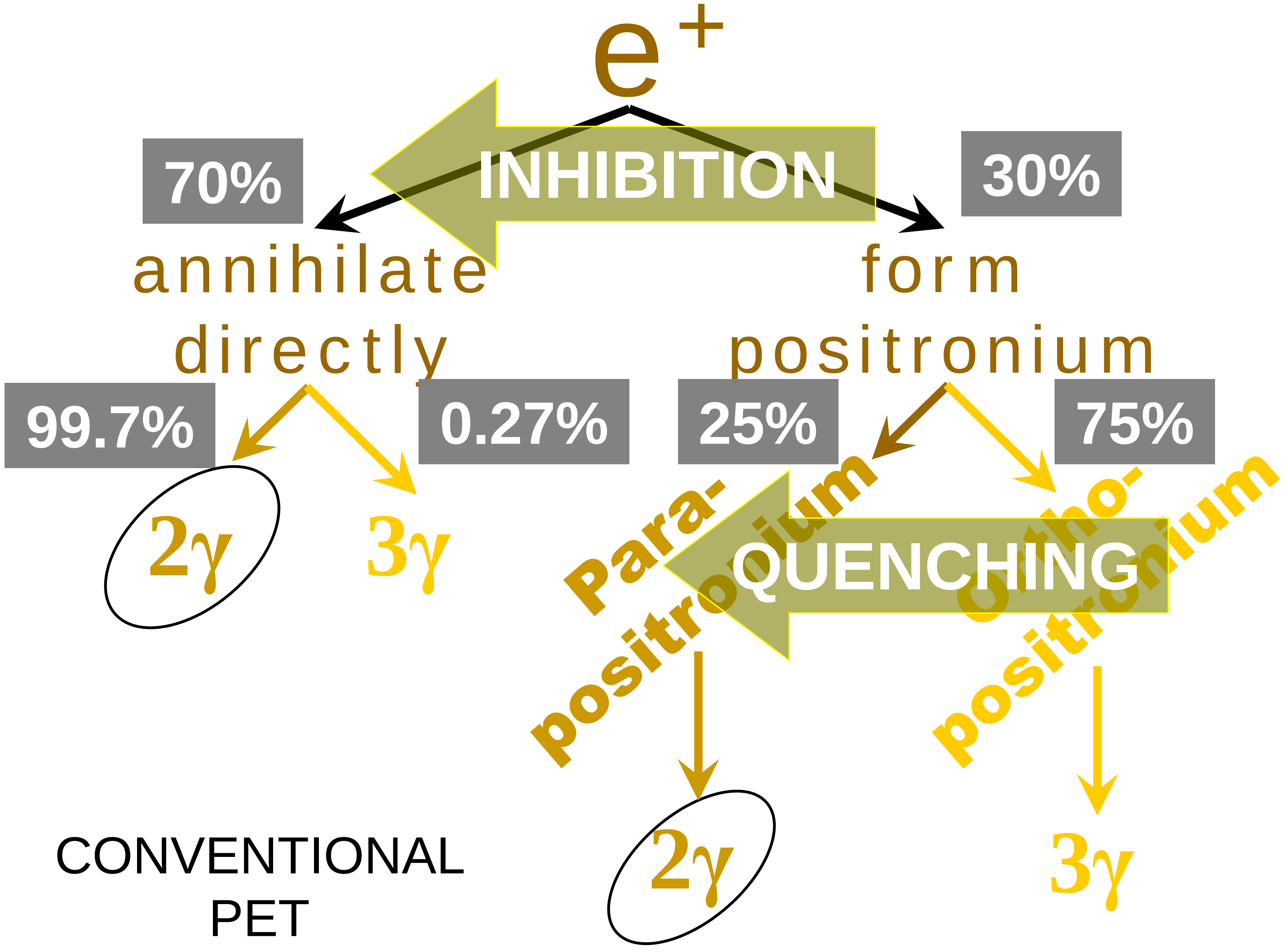
KNOWN	UNKNOWNS
(E_1, α_1) (E_2, α_2) (E_3, α_3)	(x_1, y_1, z_1)

solve simultaneous eqs

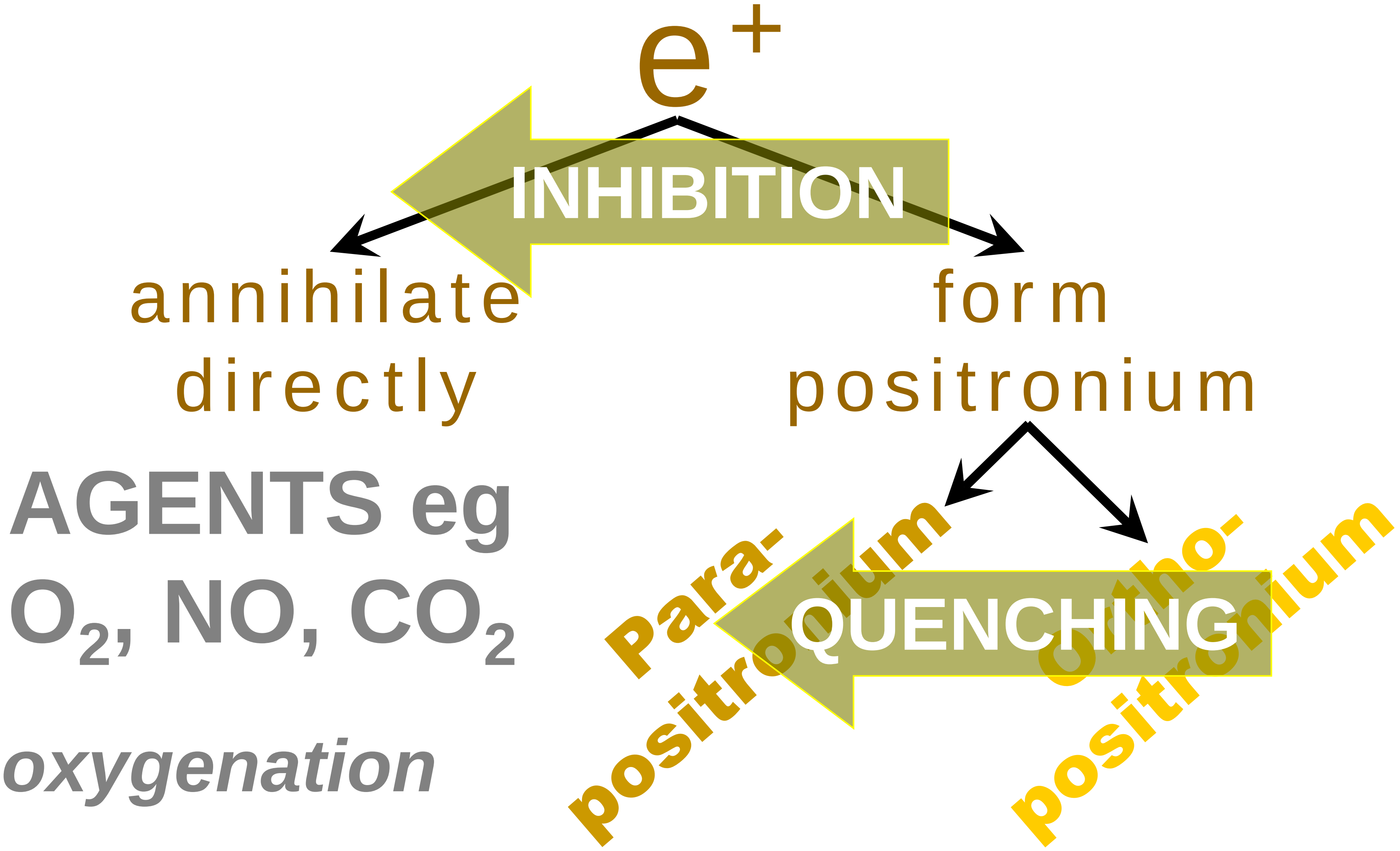
POINT OF RESPONSE



e^+
70%
30%
annihilate directly
form positronium
99.7%
0.27%
25%
75%
2γ
3γ
Para-positronium
Ortho-positronium
2γ
3γ
CONVENTIONAL PET



e+
INHIBITION
70%
30%
annihilate directly
form positronium
99.7%
0.27%
25%
75%
2γ
3γ
Para-positronium
Ortho-positronium
QUENCHING
2γ
3γ
CONVENTIONAL PET



PROSPECTS FOR MOLECULAR IMAGING

MEASURE 3γ/2γ 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.

5. Conclusions

REFUTAL

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 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).

REPRODUCED FROM MERCURIO K et al PHYS. MED. BIOL. 2006;51:N323-9

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})	$R = K_{cap}/\lambda_d$
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 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).

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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

GAMMASPHERE: AN UNPRECEDENTED LUXURY FOR US

LUXURY #1 NEAR-4π 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-4π SOLID ANGLE

LUXURY #2 MULTI-DIMENSIONAL DATA WRITTEN OUT

```
BIT - EVENT PROCESSING CONTROL BITS

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

BIT - EVENT DATA CONTROL BITS FOR EACH DETECTOR

 4   writeget              output ge time on/off
 5   writegef              output full ge data on/off
 6   writebgo              output of BGO data on/off

BIT - EVENT DATA CONROL BITS FOR EACH EVENT

 7   writeallge            output of dirty ge data on/off
 8   writeallbgo           output of clean bgo data on/off

BIT - MISC

 9   writeIsomerTag
10   rf_timing             ge times calculated vs rf pulses
                           (subtract tac2 on the fly)
```

```
GA ... NT
DA
The EVE
typedef
     {
     u_s                                                             */
     u_s                                                        ord  */
     u_s                                                             */
     u_s                                                             */
     u_s                                                             */
     u_s                                                             */
     u_s                                                             */
     u_s                                                             */
     u_s                                                             */
     u_s                                                            */
     u_s                                                             */
     u_s                                                             */
}         EVENT_BUFFER;
```

GAMMASPHERE: AN UNPRECEDENTED LUXURY FOR US

<u>LUXURY #1</u> NEAR-4π SOLID ANGLE

<u>LUXURY #2</u> MULTI-DIMENSIONAL DATA WRITTEN OUT

GAMMASPHERE: AN UNPRECEDENTED LUXURY FOR US

LUXURY #1 NEAR-4π 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 BLOOD

(HAEMOGLOBINS HAVE BEEN LIBERATED FROM RED BLOOD CELLS)

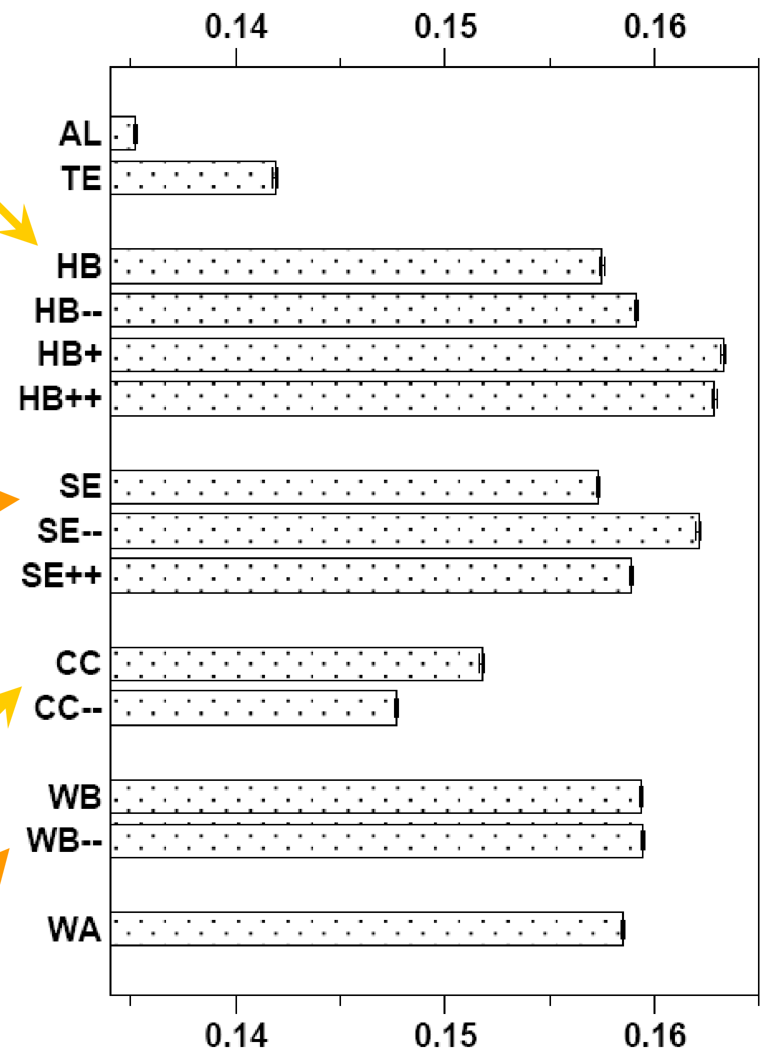
SERUM

(LIKE PLASMA BUT NO CLOTTING FACTORS)

CELL CONCENTRATE

(NO PLASMA)

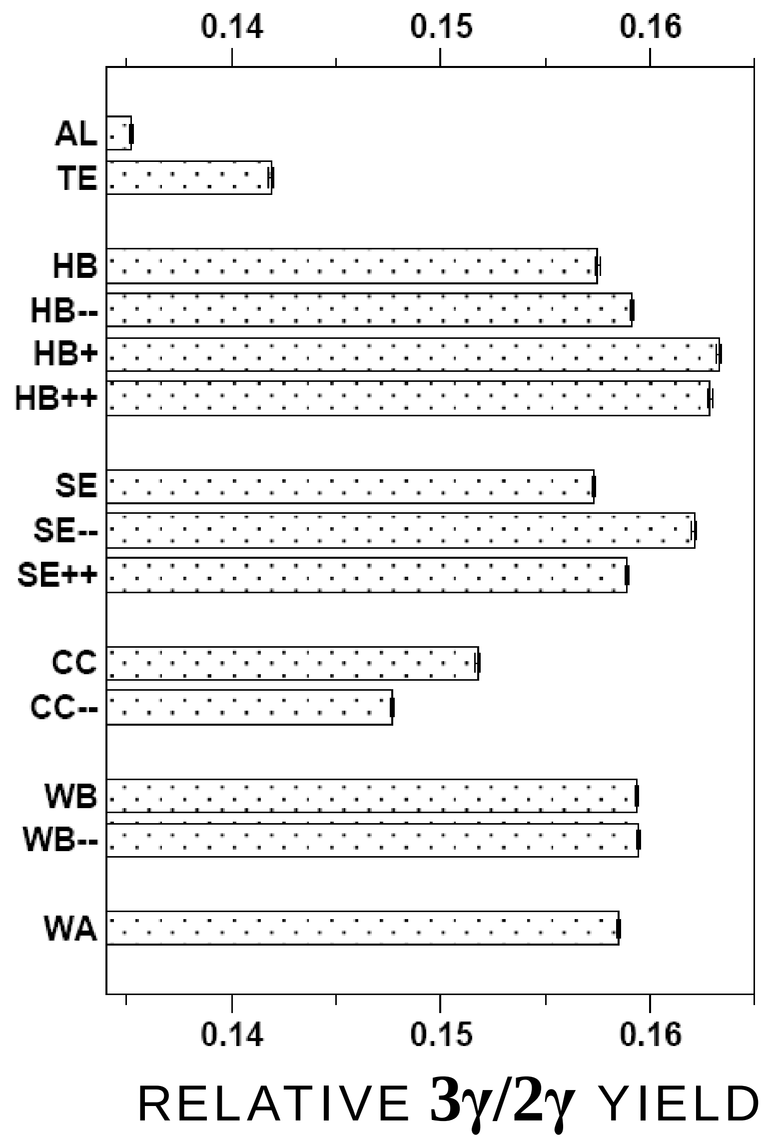
WHOLE BLOOD



RELATIVE $3\gamma/2\gamma$ YIELD

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

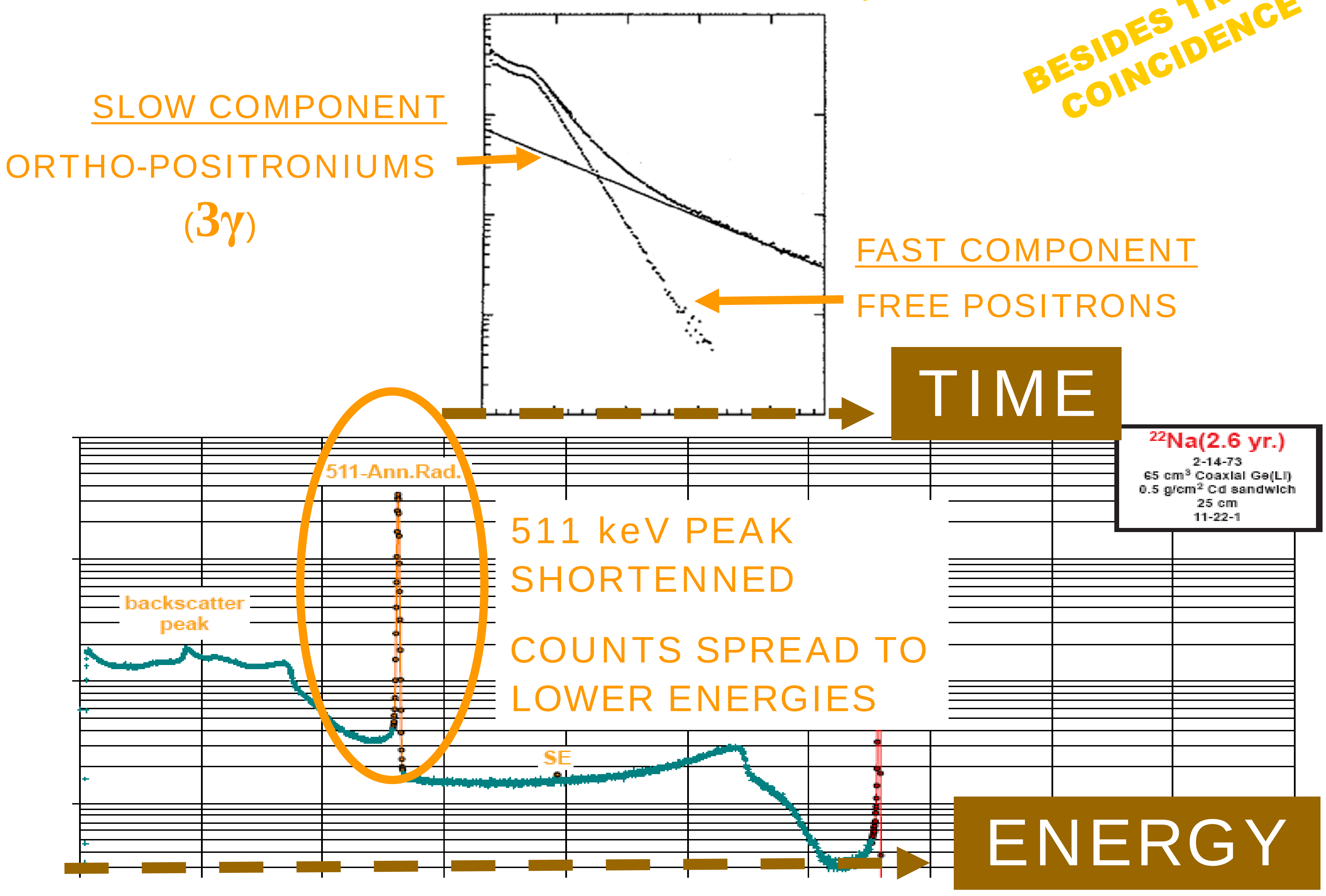


THREE-QUANTAS STUDIES:

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 3γ/2γ YIELDS



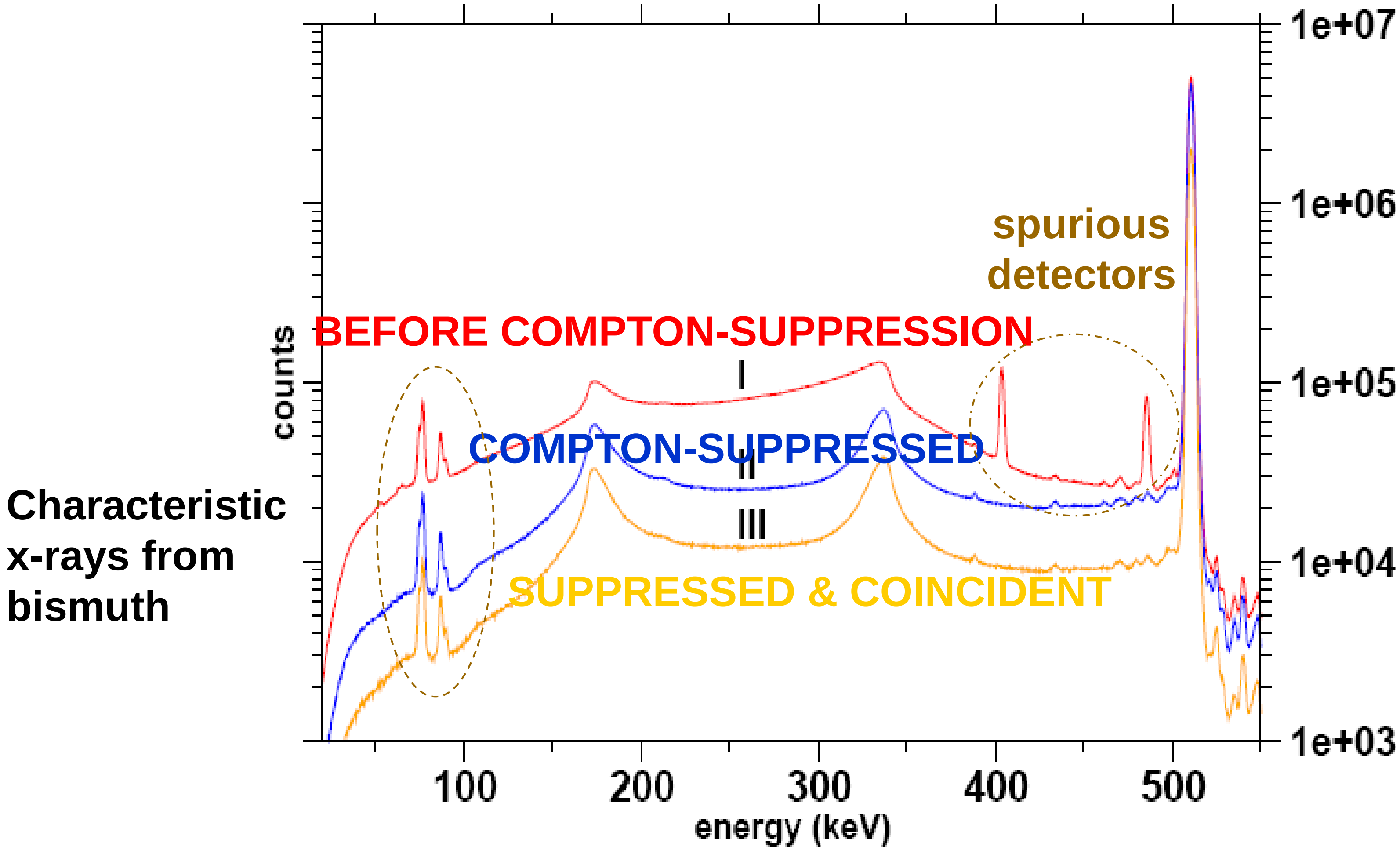
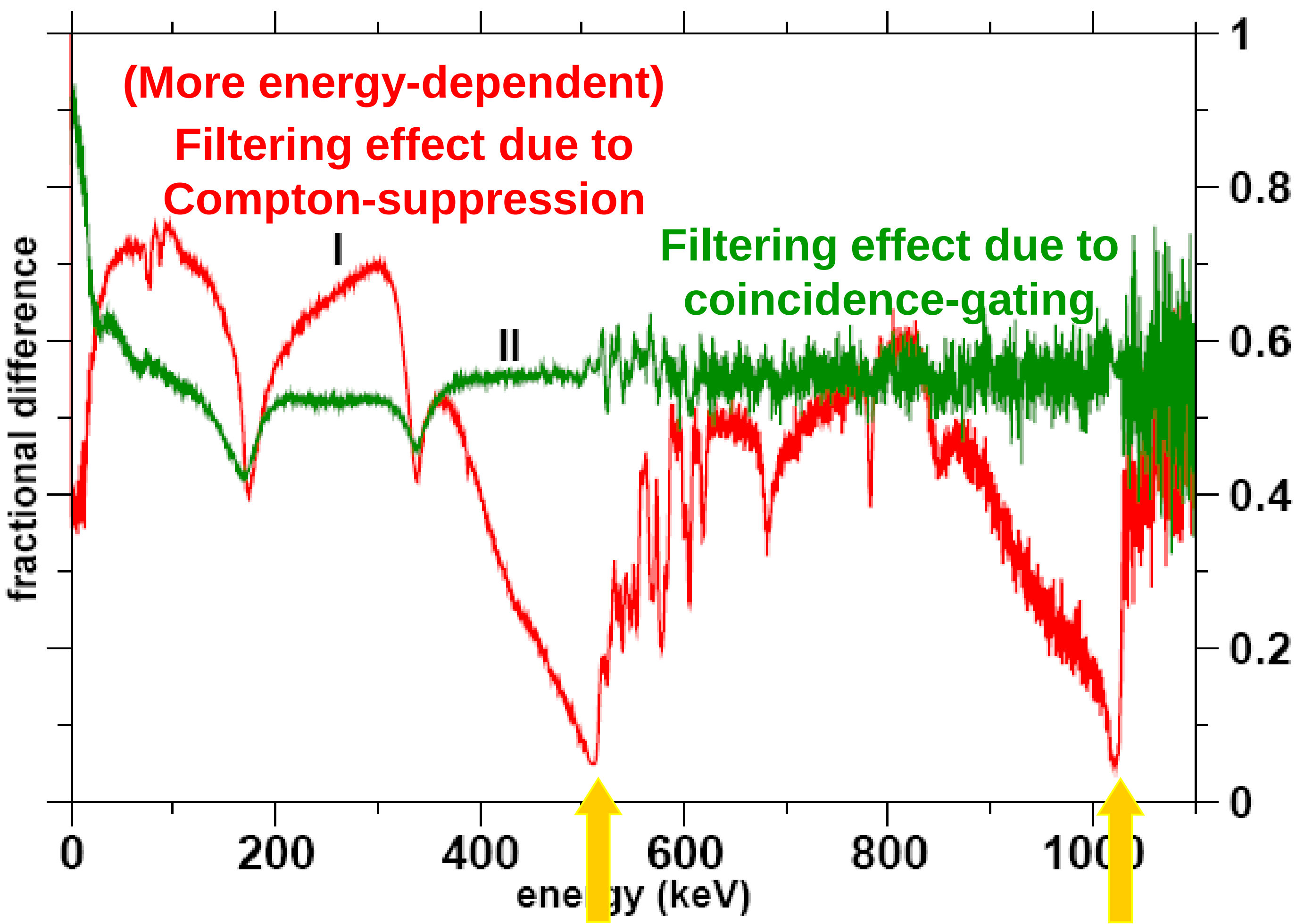


Fig. 1. Gamma spectra from the FDG source with the reference sample in place: (I) all hits from all detectors; (II) clean hits from non-outlying detectors only; (III) time-gated clean hits from non-outlying detectors only. The energy axis has been truncated.



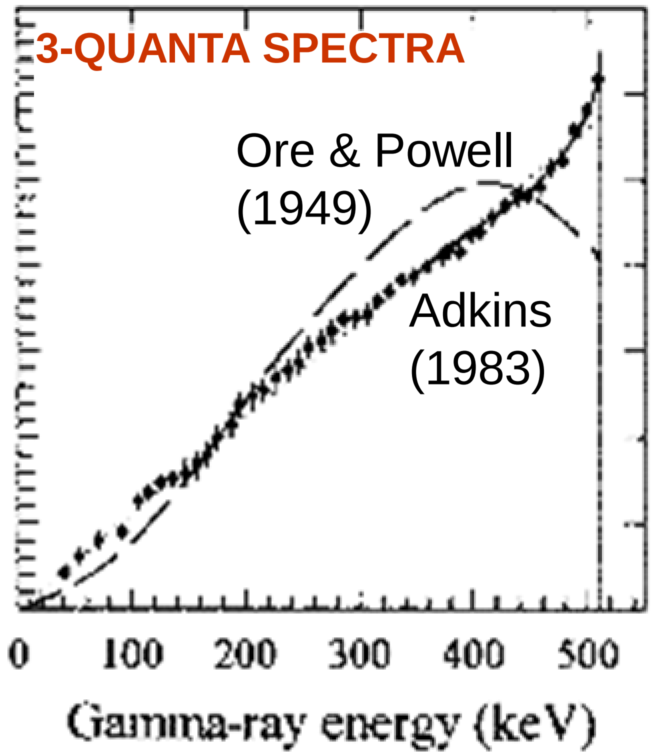
FILTERED THE LEAST: FULL-ENERGY PHOTO-PEAK & SUMMED PEAK

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

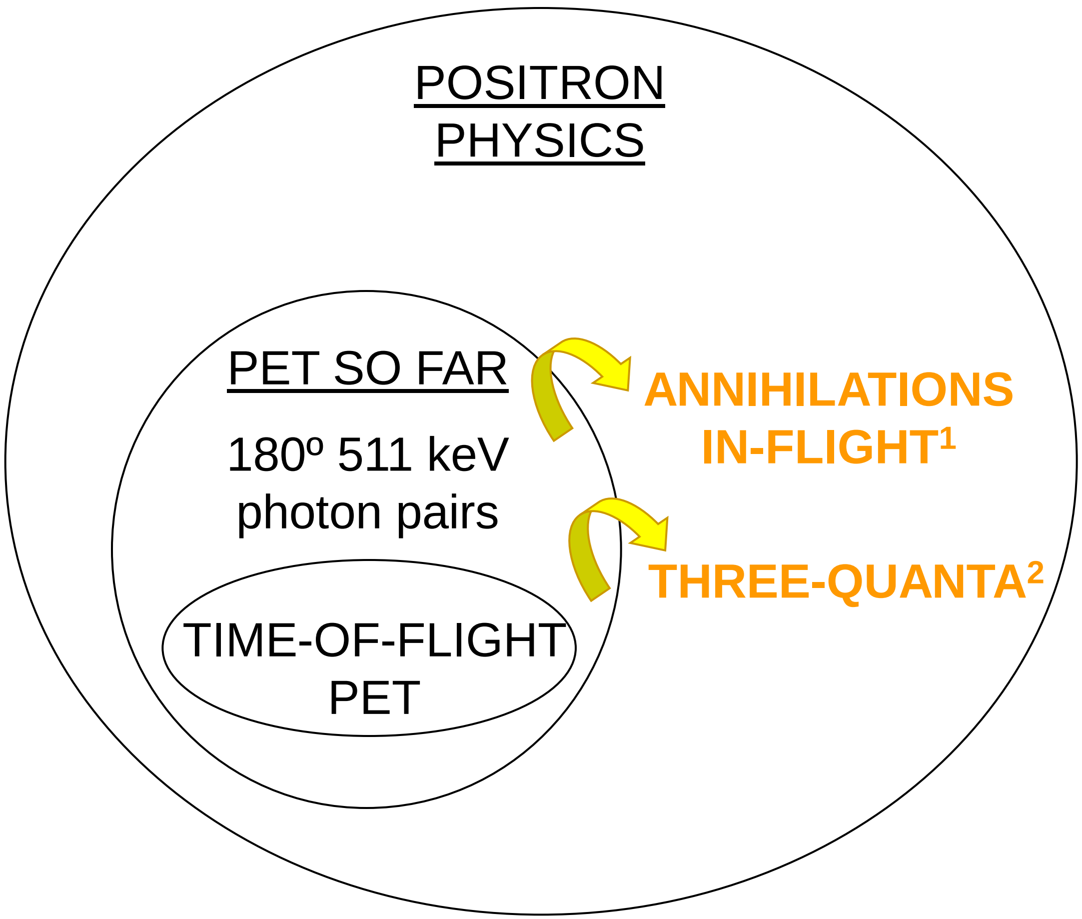
To include Compton-scattered counts instead of removing them

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!