

**LOGICAL REASONING AND REASONABLE ANSWERS  
CONSISTENT WITH DECLARED OBJECTIVES FOR THE BENEFIT OF MANKIND**

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*Abstract:* The author presents both a technological innovation and a formula that enables the balancing of the interests of business, science, and the public. Both innovation and formula are destined for those decision makers who pursue logical reasoning, who provide reasonable answers consistent with the declared objectives to benefit mankind, and who truly want a substantial reduction of premature cancer death. These innovations in PET (Positron Emission Tomography) technology, known as 3D-CBS (three-dimensional complete body screening), will facilitate the detection of cancer at an early stage, potentially saving millions of lives. Such innovations offer a significant improvement in efficiency over the 4,000 PET devices currently used in health care facilities, which cannot detect cancer at an early stage and cannot save lives. The innovations are supported by feasibility proofs, economical advantages in health care cost reduction and in great advantages for the patient. The proposed formula optimizes the power of the inter-relationships between business, science and the public interest and puts the patient as first priority, rather than prioritizing business to the detriment of the patient, while satisfying all parties involved in the solution. This article demonstrates how the “technological innovations” and the “formula” are the most promising solution to the problem of premature cancer death. The author’s solution is based on the irrefutable claim that it is possible to improve the efficiency of the 4,000 current PET devices (theoretically over 1,000 times and practically by 400 times), thus enabling the reduction of the radiation dose to permit safe screening of high risk patients and enabling identification of minimum abnormal metabolism that allows detection of cancer at an early stage when it is highly curable. Furthermore the innovation allows a lower cost per signal captured from the tumor marker, reducing examination costs, which, together with the other innovations, reduces health care cost to only \$250,000 per additional life saved from premature cancer death (versus the current cost of \$10 million per life saved), thus making the device more competitive in the market. The author presents explanations to questions asked at his seminars as to how to overcome the obstacles preventing the transfer of the benefit of innovation to the bed of the patient. For the past ten years industry has continued to build significantly less efficient imaging PET devices which cannot detect cancer at an early stage and cannot save lives, while the innovative 3D-CBS technology can prove the claimed efficiency improvement even by using material available at the time of its first publication a decade ago. It is therefore necessary to remove the obstacles of decision makers who provide “unreasonable answers” (or no answers at all), not based on “logical reasoning” consistent with declared objectives -obstacles which have delayed for over a decade the implementation of this technological solution, in spite of the numerous recognitions already obtained in the scientific and academic communities, demonstrations of the feasibility of the innovative sections proven by the author and even recently by experimental results obtained by industry (i.e., Siemens). Due to the importance of this seminar to the world, it is expected that by presenting this article during the series of courses on “Planetary Emergencies,” broad enough awareness will finally be created about the validity of the author’s scientific arguments that could already have saved many lives. Doing so, shortly we will be able to say that everything possible has been done to increase the efficiency of current PET targeted to early cancer detection by implementing in a single giant step all the innovations of the author that could have already benefitted mankind for a decade.

## **1. Identifying Social Objectives**

Statistical data show that during the past half century the heart disease death rate has been cut by more than half while there has not been a substantial reduction in the cancer death rate [1]. Cancer kills prematurely (under age 75) one person in the world every 5 seconds [2], one every 100 seconds in the U.S.

The FDA (Food and Drug Administration) Deputy Commissioner stated in his Nov. 29, 2005 speech: “The total amount that we are investing in research into new medical products and specifically new medicines easily tops \$100 billion and by some estimates approaches about \$150 billion every year. Clearly there is a disconnect between the resources we’re devoting to developing new medical products and what we’re getting in return in the way of new and better treatments.” Americans spent \$179 billion on prescription drugs in 2003 - that is up from \$12 billion in 1980 [3].

According to publications by Annual Review of Public Health, American Cancer Society and Bureau of the Public Debt [4], the economic cost of cancer treatment indexed to 100 in 1963, increased to 5,000 in 2003. This can be compared with the U.S. national debt that increased in proportion in 2003 only to 2,300 and the price of gasoline in U.S. increased to 500.

Clifton Leaf in Fortune magazine March 22, 2004 [6] states: "...That is also the devastating conclusion of a major study published last August in the *British Medical Journal*. Two Italian pharmacologists [Silvio Garattini and Vittorio Bertelé [5],] pored over the results of trials of 12 new anticancer drugs that had been approved for the European market from 1995 to 2000, and compared them with standard treatments for their respective diseases. The researchers could find no substantial advantages — no improved survival, no better quality of life, no added safety — with any of the new agents. All of them, though, were several times more expensive than the old drugs. In one case, the price was 350 times higher."

The U.S. alone has spent over \$200 billion on cancer research during the past 40 years and according to PubMed, a National Cancer Institute (NCI) online database, the cancer research community has published 1.56 million papers as of 2004 [6].

In spite of these impressive numbers, a significant reduction in premature cancer death has not been achieved; therefore it is essential to focus on this social objective.

## 2. The Most Promising Intervention for Substantially Reducing Premature Cancer Death Now

The irrefutable key to cancer survival in most cases is early detection. Experimental data show that **cancer is curable and life is saved in 90% to 98% of cases when diagnosed at an early stage** [7], [8], [9], [10]. Given such a promising result, **the most logical solution to significantly reduce premature cancer death now is to target the improvement of early detection through a safe, economical and noninvasive medical diagnostic method**. Such a method would ideally be capable of identifying the development of the very first cancerous cells with high sensitivity and accuracy in order to avoid "false positives" and "false negatives."

In over a half century of research, no drug has been developed that can claim to achieve a similar, substantial reduction in overall cancer death rates when compared to early detection. So while the discovery of drugs that attempt to cure late-stage cancer is critical and should continue to be pursued, it is equally imperative that the scientific research community continue to explore every possible cancer prevention and detection alternative with the utmost diligence.

Regrettably, although early detection is the valid solution, data shows that it has not been pursued adequately.

## 3. Comparison of Current Medical Diagnostic Technologies

Cancer manifests itself in various ways. It can cause a change in tissue density, in temperature, in cell structure and/or in nutrient consumption rate (metabolism) of the cancerous cells. Devices have been built to visualize information based on each of these properties. The most common are:

- Techniques that measure tissue density and other parameters which provide anatomical information (CT - Computed Tomography; X-ray; Ultrasound; Magnetic Resonance Imaging -MRI-; etc.) However, the development of cancer does not always show tissue density change and most tumors when detected are about 1 cm<sup>3</sup> in size, consisting of about 1 billion cells, too many to qualify as early detection. (Attempts to obtain functional imaging with CT or with MRI technology associated with contrast agents delivered to the patient are much more difficult, involve more discomfort and risk to the patient, and do not obtain the results that PET technology can provide because they are limited to showing a few specific biological processes).
- Techniques that measure the difference in temperature or fluorescence (TIR, Thermal Infrared; LIF, Light-Induced Fluorescence spectroscopy). -Such differences are difficult to distinguish, in particular for those located a few mm below the skin surface.-
- Techniques that measure the ratio between cytoplasm and nuclei of the body cells and the distance between nuclei to detect changes in structure in the tissue (histological examination). -Such techniques allow microscopic examination of cells with a resolution of one micron and observation of the result of chemical reactions with monoclonal antibodies to detect markers specific to tumors: however histological examination is invasive and cannot be used for screening.-
- Techniques that by means of cell nutrient marked with a radioisotope **measure body cell metabolism in order to detect minimum abnormal metabolism** (SPECT, Single Photon Emission Computed Tomography and PET, Positron Emission Technology). -**Cancerous cells take up to 70 times more nutrient than normal cells.**-

Of the above possibilities, it is logical to **consider most reliable the one based on the last technique because the difference [11], [12], [13], [14], [15], [16], [17] in metabolism of a cancer cell and a normal cell is high enough (from 5 up to 70 times) to be easier to detect early in its development.** This leads to the logical conclusion to invest in the technique that measures metabolism: Positron Emission Technology.

Unfortunately current PET (Positron Emission Tomography) used in health care facilities is not suitable for screening, due to the very low overall photon detection efficiency caused by geometry, electronics, detector assembly and financial factors.

In the following Sections first is described the principle of operation of Positron Emission Technology, followed by the study demonstrating the possibility of a theoretical 1,000 times efficiency improvement over current PET; finally the limits of current PET systems and the sources of photon losses are presented.

It is then imperative to identify technical-scientific objectives which are consistent with the social objective of substantially reducing premature cancer death as stated earlier. What then makes it possible to achieve the technical objectives is the author's innovative solution which overcomes the limitations of the existing 4,000 PET devices and provides the possibility to build systems capable of fast, efficient Three-Dimensional Complete Body Screening (such as the 3D-CBS) at a fully competitive cost.

#### 4. Positron Emission Technology

Positron Emission Technology is a medical imaging technique which selectively detects body cell abnormal metabolism using positron (the electron antimatter partner) emission of certain radionuclides. The relevant radionuclides are produced in a cyclotron and are used to label compounds of biological interest (also called "tumor markers"). For example, such compounds can be the normal nutrient to the body cells, such as glucose, oxygen, ammonia, etc. The labeled compound (tumor marker) is introduced into the body, usually by intravenous injection, and is distributed in tissues and organs activating the metabolic process. Because cancer cells are hyperactive, cancer-affected tissue requires more nutrient (up to 70 times) than does normal/healthy tissue (see Figure 1). This means that nutrient (labeled compound) is concentrated in the hyperactive, cancer-affected tissue, becoming in this manner an area of abnormally high number of positron emissions. Free positrons, traveling through the tissues will soon encounter an electron and undergo annihilation (collision between positron and electron). The annihilation outcome is a pair of photons fired off in opposite directions. When escaping the body of the patient, the two photons hit opposite sides of the 3D-CBS apparatus' cylindrical detector and are recorded as in-time coincidence signals. When an abnormal number of in-time coincidences originate from a localized area in the patient's body, this shows an excessive nutrient uptake for such area, like that created by hyperactive cancerous tissue, and a tumor is suspected (see Figure 2).

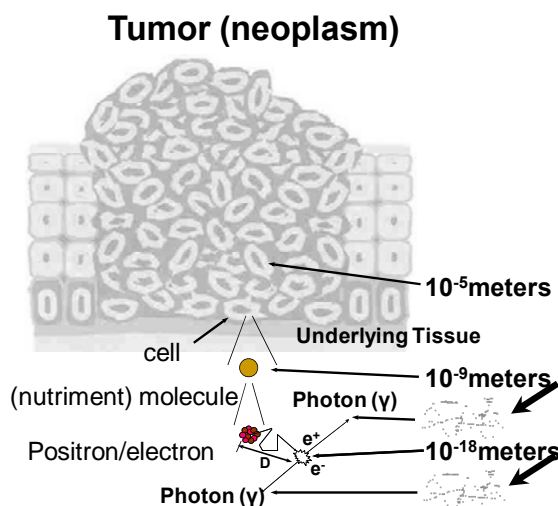


Figure 1. Representation of the cancerous tissue (neoplasm) that must be identified by its natural nutrient uptake (for example: glucose molecules) labeled with a radionuclide. The positron  $e^+$  emitted by the radionuclide, after traveling for a distance  $D$ , annihilates (or collides with) an electron generating two photons that are emitted in opposite directions and their signals detected by the 3D-CBS device.

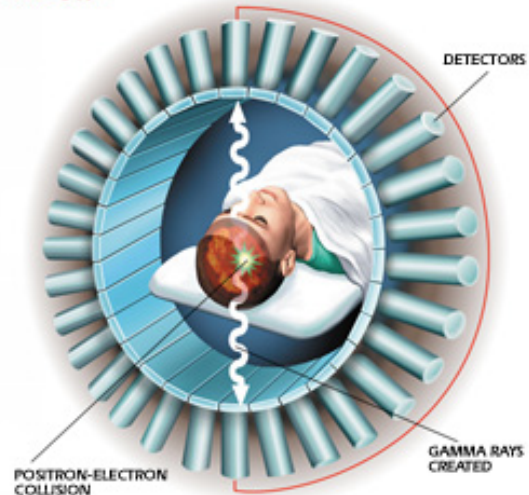


Figure 2. PET Detector. Pairs of photons (or gamma rays) hit two locations on the detector almost at the same time (called in-time coincidence). The intersection of several Lines of Response (LOR) connecting those points in-time coincidence reveal the concentration quantity of the radioisotope (or nutrient in the body cells).

Therefore Positron Emission Technology measures a consumption of nutrient, or the blood flow, not a dimension. It must count within a unit of time all possible in-time coincidences escaping from the patient's body in order to show accurately the abnormal consumption of nutrient, or the speed (or flow) of blood. It is a value related to a dynamic event, not a static event such as tumor dimension. The location (spatial resolution) where the pair of photons fired off (corresponding to the location of the concentration of the nutrient which corresponds to the location and dimension of the tumor) can also be measured very accurately, however, this is a parameter of minor importance for PET because of the random error introduced by the nuclear event of the positron making a distance of several mm (1.4 mm for <sup>18</sup>F-FDG, 4.5 mm for <sup>15</sup>O, 13.8 mm for <sup>82</sup>Ru) before encountering an electron. A very efficient Medical Imaging device based on Positron Emission Technology principle of operation can provide much more important information to the physician on how fast a tumor is growing and how aggressive it is rather than just providing its dimensions. Furthermore, such a technique is not limited to show only abnormal metabolism, but it can provide to the physician precious information about any biological process that can be tagged with a radioisotope. The more efficient the device is, the earlier an anomaly can be detected.

Because the labeled compound is radioactive, it is capable of causing damage to body cells. This must be minimized. A compromise needs to be made between giving a sufficient radiation dose to detect abnormal metabolism and keeping the dosage low enough to minimize potential damage to the body cells. (The International Commission for Radiation Protection –ICRP– recommends not exceeding 100 mrem for screening on asymptomatic patients). The best performance can only be achieved if the largest possible number of annihilations (generating pairs of photons in-time coincidence, or “signals”) is identified and measured accurately. Consequently the use of Positron Emission Technology for annual cancer screening of asymptomatic people at high risk requires the highest possible efficiency of the device that should capture the maximum number of pairs of photons in-time coincidence (signals) using the lowest possible radiation dose.

The author's innovative 3D-CBS technology (3-D Complete Body Screening) [18], [19], has the goal of providing information about the smallest indication of abnormal metabolism with the lowest possible radiation dose and cost to the patient. This objective is technically achieved when the maximum efficiency in detecting in-time coincidences (signals) is attained.

### 5. Theoretical efficiency: 1,000 times improvement

The theoretical number of pairs of photons in-time coincidence generated by the positron-electron annihilation that can be captured by detectors of different length (FOV) has been reported in several scientific articles [20], [21], [22], [23], [24] and is represented by the curve shown in Figure 3.

The graph shows that theoretically the number of counts per second can be increased from about 50,000 per second (bottom left) to about 50 million per second (top right). The example shows, for an activity of 10 mCi, e.g., the approximate calculation of the number of pairs of photons in-time coincidence that hit detectors with different FOVs, assuming a patient of about 170 pounds. Fewer photons will hit the detector for heavier patients, while more photons will reach the detector for a smaller patient.

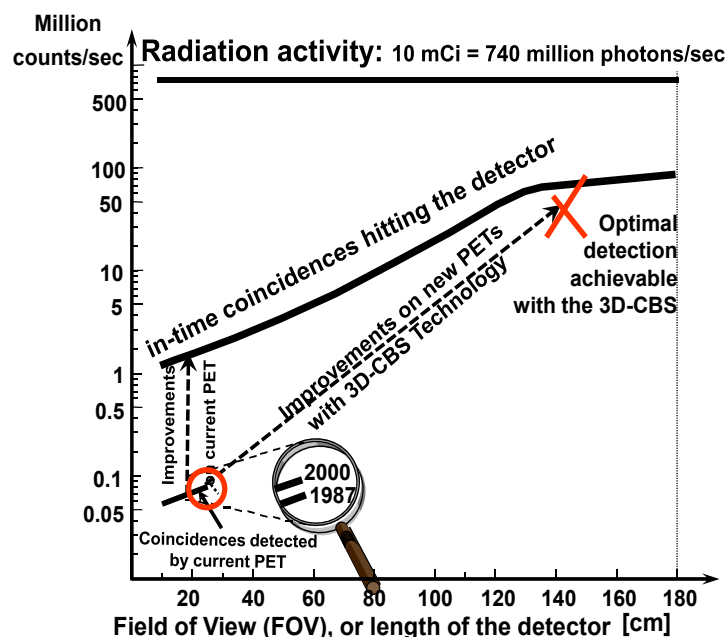


Figure 3 Graphic representation of the actual in-time coincidence detection capability of current PET vs. the theoretical limit that new PET/CT detectors should attempt to achieve. The 3D-CBS aims to approach the theoretical limits in one giant step instead of providing small incremental improvements of efficiency every few years (two to three times improvement every five years), as has occurred during the past decades. The major area in need of improvement are the electronics, a different, simplified detector assembly, and the capability of executing complex real-time photon detection algorithms (vertical arrow, left on figure). Additional improvements can be achieved as a result of the combination of the innovations implemented in those area. This will allow the use of more economical crystals that allow increased FOV (inclined arrow to the right) keeping the entire device at a reasonable cost. (See Figure 6, Sections “r,” “i,” “l” and “o” for more information about the innovations).

## 6. Limits of Current PET

Over 4,000 current PET (Positron Emission Tomography or PET/CT) devices are in use today globally, having cost over \$2 million each. However, these diagnostic devices are severely limited since they are capable of capturing (although inaccurately) only 1 out of every 10,000 signals emitted by the tumor markers attached to the molecules of body cell nutrient. This low efficiency does not allow early detection because it cannot measure minimum abnormal metabolism; consequently tumor size must be large to be detected.

Limits in efficiency due to the construction of current PET are detailed in several articles [25], [26], [27], [28], [29]. This low efficiency also requires a high radiation dose, which is hazardous to the patient and makes it unsuitable for annual screening of asymptomatic people at high risk. Therefore it has a limited chance to save lives.

One of the limits is caused by the use of the “block detector” that does not allow improvement of the signal-to-noise ratio even when more sophisticated electronics are used as shown in Figure 4.

The block detector of current PET consists of four PMT tubes coupled to a set of crystals (64 in the figure example). Slits of variable lengths (made of reflecting material) in the crystal act like a light guide that allows more or less light sharing between the four PMTs. The long slits of reflecting material at the edges of the 8x8 crystal block allow minimal or no light sharing between adjacent 8x8 crystal blocks (or 2x2 PMT blocks). The identification by the crystal of interaction in the 2x2 PMT block is made through the Anger logic shown at the bottom right of the figure. The crystals at the edges and corners of the 8x8 crystal block contribute a smaller signal compared to the inner crystals, making their identification more difficult.

More specifically, edge crystals have relatively poor light collection, and therefore, poorer energy resolution. Spatial resolution, in fact, suffers at the edge of each 2x2 photomultiplier (PMT) block because the centroid algorithm cannot weigh the PMT signals from both sides of the PMT closest to the point at which the photon struck the crystal. This causes a reduction of the overall sensitivity, which translates into greater patient exposure to radiation, poorer image quality, and longer scanning time.

The 3D-CBS assembly solves these problems by permitting all crystals to have the same degree of light sharing with adjacent crystals with slits of equal length (or no slits). This allows for sharing the light with adjacent PMTs in the four directions with no boundaries. The interconnections in the North, East, West, and South directions of the electronic channels of the 3D-Flow system allow any PMT receiving the highest signal to be identified as the center of a 3x3 (or a 5x5) cluster which then rebuilds the total energy of the incident photon by summing all the adjacent signals and by calculating the centroid.

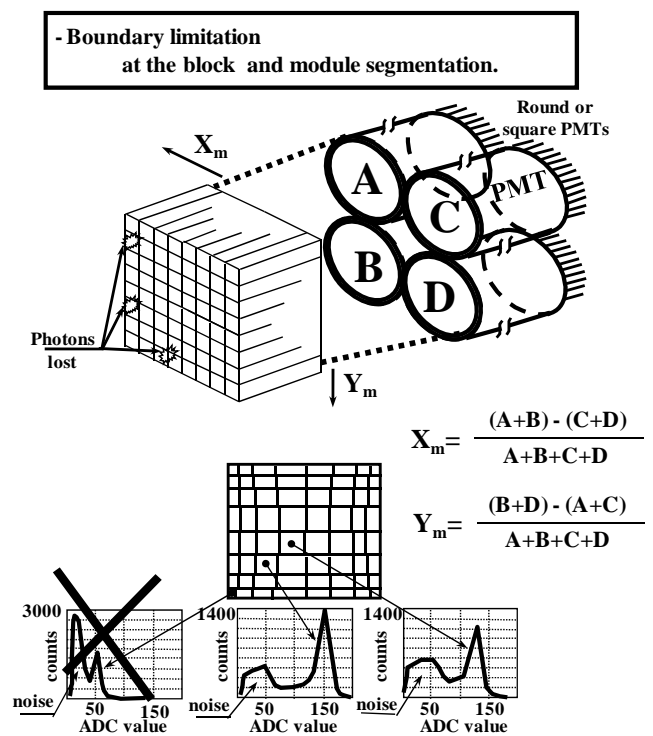


Figure 4. Inefficiency of the “block detector” used in current 4,000 PET

## 7. Where the photons are lost in current PET

Before attempting to improve any system, it is necessary to determine where the inefficiencies are, how great they are, how they can be reduced, and by how much. A detailed study of where the photons are lost in current PET is described in Figure 5 which is divided into six sections as follows:

**Overall loss:** The initial number of pairs of photons emitted per second by the tracer in the patient’s body (1,424 million/sec), represented in the upper left of Figure 5, and the number of pairs of photons per second captured by current PET (0.2 million/sec), represented in the lower left of Figure 5 are not in question, because those quantities have been measured by hospitals and universities and are in accord with the measurements made by PET manufacturers [30].

**Section (1): Photons lost in the patient’s body:** Of the initial quantity of pairs of photons emitted from within the body, some 1,210 million pairs per second are scattered or absorbed in the body. Only 214 million pairs per second leave the body. This quantity of capturable photons, equivalent to 15% efficiency for the first stage, is supported by several simulations made by scientists at Los Alamos Laboratory and at universities in California and elsewhere [20], [21].

**Section (2): Field-of-view (FOV):** Photons from outside the detector area are lost, yielding an efficiency percentage figure equivalent to 8.5% for this stage. Applying this percentage to the 214 million pairs of photons per second leaving the body, only 18 million capturable pairs per second remain.

**Section (3): Solid angle:** Some photons from within the detector area are also lost. Only 3.2 million pairs of photons per second remain to be captured after stage 3, which is equivalent to 18% efficiency for this stage.

**Section (4): Detector stopping power:** Detector crystals do not have perfect stopping power and not every photon entering the detector interacts within it. After stage 3 in some low-cost crystal detectors, 20% are lost or 0.6 million, and 80% remain potentially detectable, or 2.6 million pairs per second.


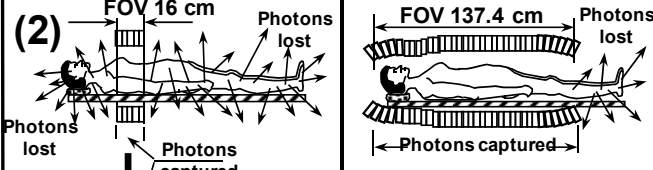
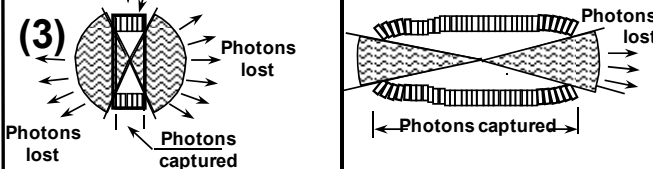

Changing the role of PET to screening for cancer									
Current PET systems					PET capabilities with 3D-CBS				
Process affecting capture/loss of photons	Photons MBq		Efficiency at each stage	Radiation dose		Efficiency at each stage	Photons MBq		
	Remaining	Lost		Reduced to 3%	Lost		Remaining		
<b>Radiation dose</b>	1,424			Inject 66 mCi of <sup>15</sup> O-water = 1,424 MBq (at start of exam)	Inject 2.2 mCi of <sup>15</sup> O-water = 47.4 MBq (at start of exam)			47.4	
Photons at start of scanning not scattered and/or absorbed in the body	214	1,210	15%	7% to 25% pair of photons in time coincidence leave the body <b>(1)</b> 		15%	40.3	7.1	
<b>Field-of-view (FOV)</b> (photons from outside the detector area are lost)	18	196	8.5%	<b>(2)</b> 		95%	0.4	6.7	
<b>Solid angle</b> (some photons from within the detector area are also lost)	3.2	14.8	18%	<b>(3)</b> 		92%	0.5	6.2	
<b>Stopping power (SP)</b>	2.6	0.6	80%	<b>(4)</b> Crystal photon detection capability 		80%	1.2	5	
<b>Electronics</b> (photons captured)	0.2	2.4	8%	<b>(5)</b> Limitation of the electronics of current PET to identify “good” photons		95%	0.3	4.7	
				<b>(6)</b> Limitation of the electronics of current PET to identify photons in time coincidence					
<b>0.014% Efficiency</b>					<b>0.2 million coincidences/sec found</b>		<b>4.7 million coincidences/sec found</b>		<b>10% Efficiency</b>

Figure 5 shows the difference in efficiency between the current PET (left) and the 3D-CBS PET with the 3D-Flow™ (right). Areas of inefficiencies are detailed in Sections 1 through 6. Only the innovation of the electronics in sections 5 and 6 allow for the improvement in efficiency, in a cost-effective manner, in sections 2 and 3. (The column of MBq = million of pairs of photons per second, shows the numbers of photons lost and photons remaining at each Section, and the reduction applied as a percent of efficiency for that Section is found in the adjacent columns). Although the figure shows a possible increase in efficiency greater than 400 times, a conservative estimate of 400 times is pursued to achieve the goals of reduction of radiation to the patient to allow safe annual screening, to achieve early detection, all at a reasonable cost.

**Sections (5-6) Electronics (combined with detector assembly):** Calculation by default. Current PET capture only 0.2 million pairs per second of the original 1,424 million pairs of photons per second emitted by tracers within the patient’s body (see measurements made by PET manufacturers and universities reported in scientific journals such as Figure 9 of reference [30]). Of the 2.6 million pairs of photons per second remaining after stage 4, the loss of 2.4 million pairs of photons per second is accounted for by deficiencies in the electronics and the detector design. The efficiency of stages 5 and 6 can be calculated as equivalent to 8%, as derived by subtraction from the total inefficiency and the sum of the other inefficiencies.

It is obvious from this analysis that the section that needs serious study and improvement is the last one which provides only 8% efficiency. Section 1 has efficiency related to a natural phenomenon that cannot be changed. The losses of Sections 2 and 3 can be addressed by increases in length and solid angle only if the electronics of sections 5 and 6 are not overwhelmed by the increased amount of data to be analyzed. Although Section 4 denotes the area in which much effort and money has been invested during the past decades, crystal efficiency has been at 95% for the past half century, some (such as LSO) have nearly ideal characteristics and there is not much room for further improvement. (In Figure 5 some low-cost crystal detectors with 80% efficiency have been considered).

### 8. Identifying Technical-Scientific Objectives

A constant goal in medicine is to identify abnormal biochemical activity associated with a specific pathology and to observe the abnormality directly as soon as possible in the diseased organism.

Cancer is detected unequivocally in most cases using histological invasive examination revealing information about changes in shape, structure, metabolism and other biological processes of cancer cells. However, the challenge is to achieve unequivocal detection with a non-invasive procedure.

In other words, the fundamental goal of technological research should be to provide physicians with a **non-invasive means to diagnose cancer with a level of accuracy similar to that obtained with histological examination**. The technique should also be safe for the patient, economical and should detect cancer cells at a very early stage of development, targeted to detect minimum abnormal metabolism.

Such a technique and its characteristics when compared to current PET are shown in Table I

Table I Specifications for PET of Type A and Type B

<b>Type A (current PET)</b>	<b>Type B (New 3D-CBS)</b>
<b>Medical Imaging Device at the molecular level (the one that does not allow early detection: Patient is not first priority)</b>	<b>Medical Imaging Device at the molecular level (the one that can save lives: Patient is the very first priority)</b>
<ol style="list-style-type: none"> <li>1) Low cost of manufacturing the machine is important for maximizing profit</li> <li>2) Optimized for measuring spatial resolution (to measure the shrinkage of a tumor for drug usage purposes)</li> <li>3) Low efficiency (for the same reason as above, only measuring tumor shrinkage)</li> <li>4) High radiation dose deemed acceptable as it is only for seriously ill patients</li> <li>5) Long examination times (more than one hour to acquire data from 140 cm)</li> <li>6) High cost of the examination (due to long exams times and high radiation dose) deemed acceptable as seriously ill patients or their insurance will pay. Competition could be sustained by playing on the following parameters: higher radiation dosage to the patient, scanning a smaller section of the body, recording fewer data which allow detection of tumors at an advanced stage only</li> <li>7) Short detector is less expensive but results in long exam times and low efficiency</li> </ol>	<ol style="list-style-type: none"> <li>1) Low cost of the examination (achieved by lowering radiation dose, and shortening examination time with a more efficient device) necessary for repetitive exams on ill patients and annual exams on asymptomatic patients</li> <li>2) Low radiation dose and short examination times (about 4 minutes) necessary to allow screening and repetitive exams on ill patients</li> <li>3) Very high efficiency (able to count more photons, detect the very first cancerous cells and preempt metastasis)</li> <li>4) Optimized for measuring sensitivity (same reason as above, preempting metastasis)</li> <li>5) Long detector is more expensive but results in short exam times and higher efficiency because it acquires many data points simultaneously and oblique photons from the entire body</li> <li>6) Higher cost of the machine is acceptable if it is sufficiently more efficient</li> <li>7) Short time to recoup investment (because more patients can be examined per day)</li> </ol>

### 9. Key innovations of the 3D-CBS technology

A solution for safe screening targeted at early cancer detection has been in existence for over a decade, documented in several publications by the author [18], [19], [28], [29], [31], [32], [33], [34], [35], [36], [37]. It is an innovative technology that allows building a device over 400 times more efficient than current PET. Figure 6 summarizes the author's innovations described in more detail in the references.

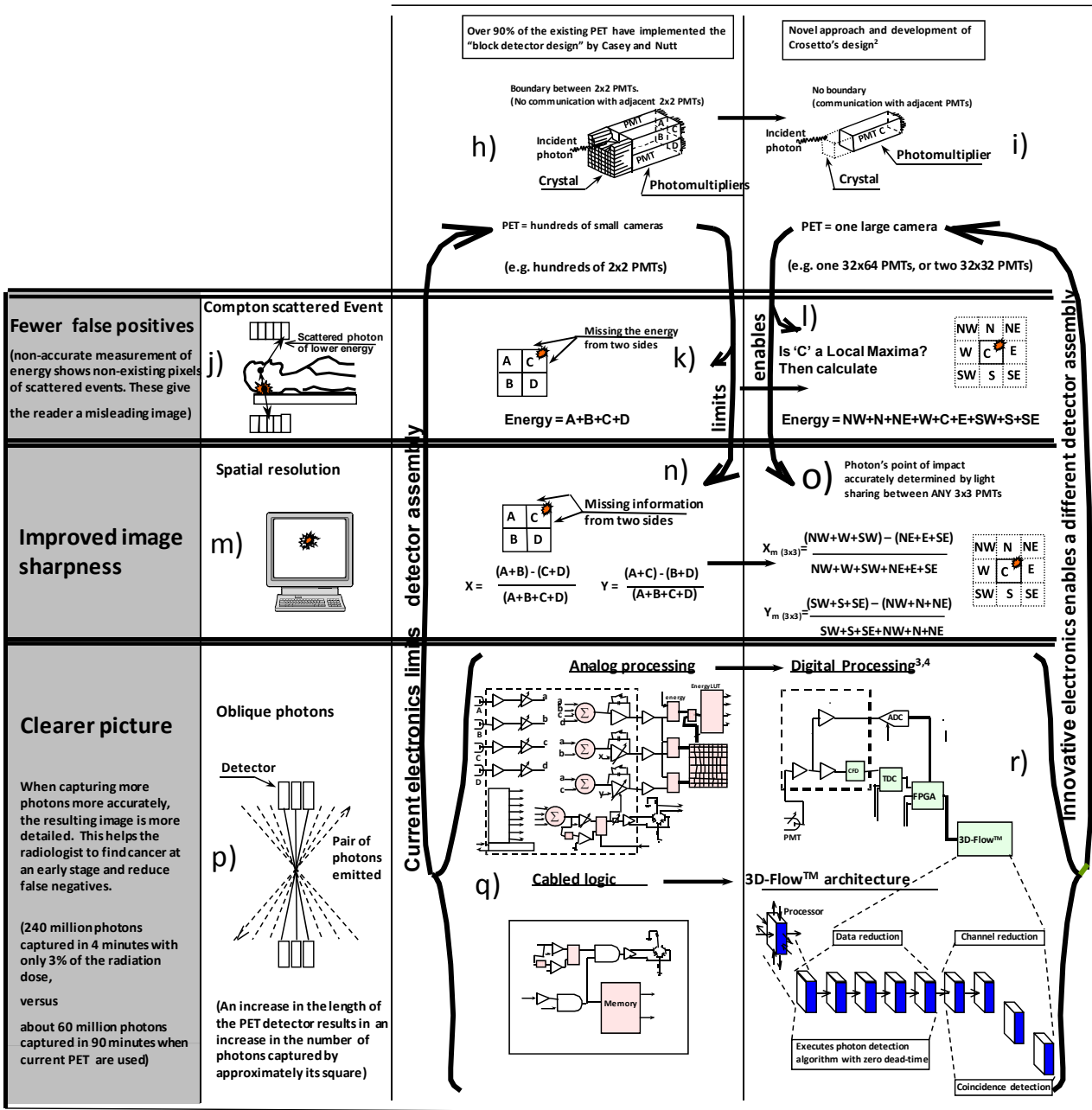


Figure 6 The three titles in the left column summarize the advantages important to the doctor/radiologist compared to current medical imaging devices. Each title is illustrated in the adjacent column and in the two remaining columns to the right are compared the limitations of current technology, and the improvement achievable with 3D-CBS. See Sections j, k, and l for energy resolution; m, n, and o for spatial resolution; and p, q, and r for sensitivity. The key innovations start from the feature in Section "r," which enables the innovation in Section "i," which in turn enables the innovations in Sections "l" and "o." (Additional innovations are achieved as a result of the combination of these).

One example of the implementation of this innovative technology is in the construction of a cost-effective apparatus called 3D-CBS (Three-Dimensional Complete Body Screening).

#### a) Author's claims:

The author claims that his innovation allows capturing over 400 times the number of photons emitted by the tumor markers arriving from the body of the patient compared to the number of photons captured by current 4,000 PET when the same radiation activity is present in the patient's body. Furthermore, the photons are captured by the innovative 3D-CBS technology more accurately in terms of arrival time, spatial resolution

(x, y, z) and energy resolution, and at a lower cost for each photon captured. Innovations are also in the area of displaying results in a more accurate manner to the physician. These advantages permit considerable reduction of the radiation dose administered to the patient, enable early detection of anomalies and avoid misdiagnosis of “false positives” and “false negatives.”

**b) How claimed objectives are achieved with the author’s innovations**

The key elements of the author’s innovative technology that allows building a device of the type 3D-CBS are in five main areas: electronics, which enables innovations in a different, simplified detector assembly, which in turn enables the innovations in the capability of executing complex real-time algorithms. Additional innovations, such as the ones that enable the use of more economical crystals that allow increased FOV keeping the entire device at a reasonable cost, can be achieved as a result of the combination of the previous innovations. The following is a schematic list of the most important innovations and their outcomes (see also Figure 6):

1. Innovative electronics providing a means of:
  - a) accurately measuring the impact point and energy of oblique photons
  - b) reducing the initial number of the electronic channels, and
  - c) simplifying the method for identifying in-time coincidences
2. Improved and simplified detector assembly
3. Capability of executing precise algorithms for photon identification
4. Increased detector length – longer Field of View (FOV)
5. Innovations in the visualization of the information obtained (Section 9, Figures 2, 3 of [20])

The synergy of coupling several innovations, such as in the detector, sensors and the electronic system, enables execution of real-time algorithms for more accurate and efficient photon identification at a lower cost per photon captured.

The advantages are summarized in Figure 7.

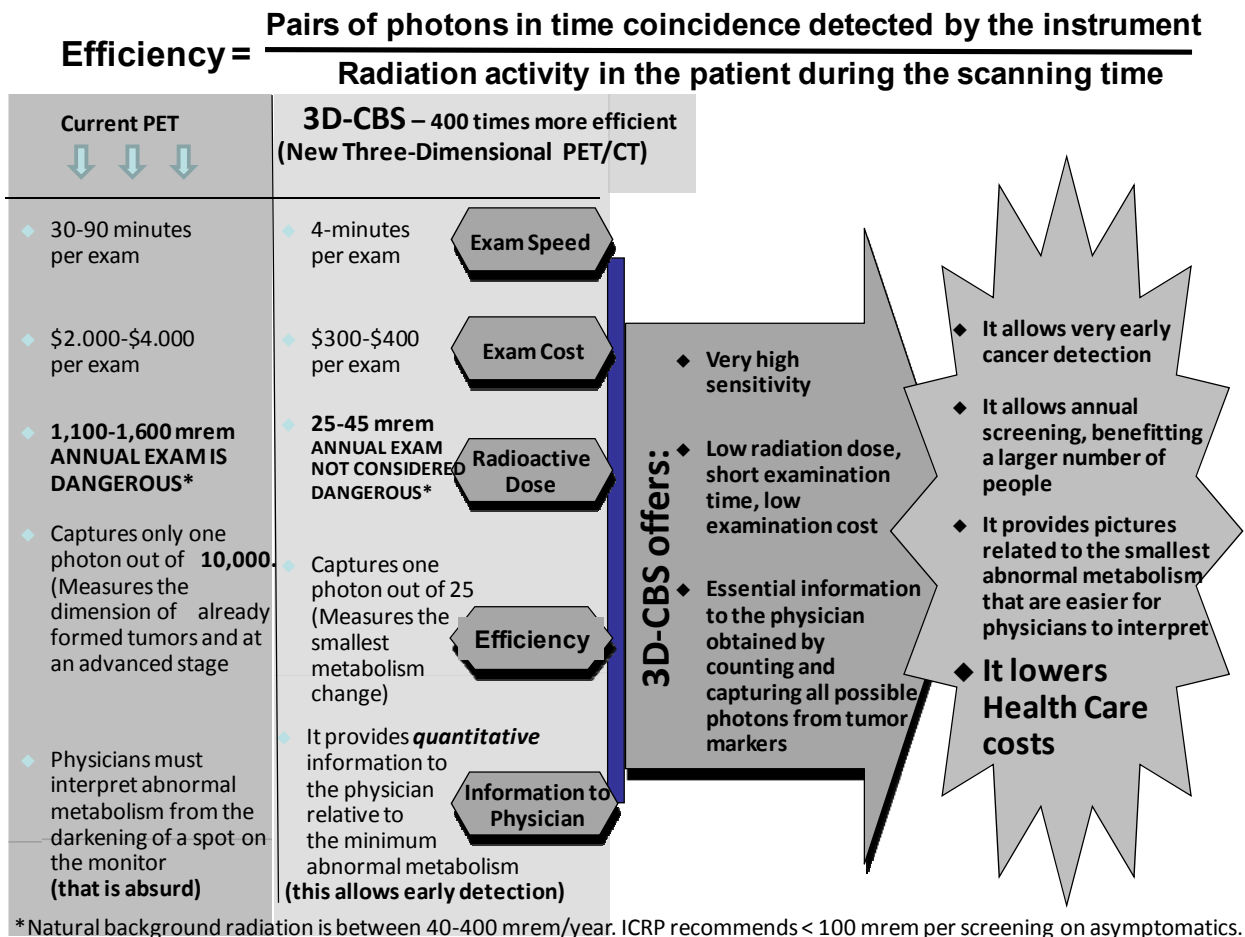


Figure 7. Advantages of the 3D-CBS innovative technology.

### c) *Experience in solving similar problems at SSC (TX) and LHC (CERN) experiments*

The author has solved similar problems for the top experiments in High Energy Physics (HEP) during his career at CERN (European Center for Particle Physics) in Geneva and at the Superconducting Super Collider (SSC) in Texas.

The common problem in HEP experiments and PET medical imaging devices is to discriminate between “good” events and the background (called here with a more generic term “noise”) which, in HEP experiments, can be several orders of magnitude larger than the signal. In the PET environment, the “signal” consists of a back-to-back pair of 511 KeV photons hitting simultaneously opposite crystals within the detector. In HEP experiments the selection of interesting events is usually performed in various stages, the first one being usually referred to as “First-Level Trigger”. In PET devices the event topology and particle multiplicities are much more manageable, and, with a suitable choice of electronics, full event selection can be performed in a single step. In both cases this unit that we call with a more generic term “decision box” (or trigger) should have the capability to selectively recognize within hundreds of nanoseconds, the signals of a “good event” by analyzing (by executing a First-Level Trigger algorithm) a set of many signals arriving from thousands of channels at a very high rate. Because in nature these “good events” occur randomly, the “decision box” must be capable of capturing and processing two (or more) sets of thousands of signals separated anywhere between a few to hundreds of nanoseconds. The more efficient the decision box is in capturing and measuring very accurately the characteristics of the possible “good events”, the less radiation is needed and the more chances there are to recognize abnormal metabolisms.

The author was invited in 1991 to work for one HEP half-billion dollar experiment at SSC (GEM-Gamma Electron and Muon) to solve such kinds of problems for the First-Level Trigger algorithm of that specific experiment -in competition with SDC (Solenoid Detector Collaboration) at SSC and other equally complex experiments at CERN (Geneva) LHC (Large Hadron Collider).

Very unusual for entities working in competition, but very appropriate in interpreting the pure essence of how research should progress to the benefit of mankind, the author asked his supervisors for a paradigm change in the way research for a solution to a problem in that field is usually carried out and specifically if he could think outside the box and try to conceive a solution that would be beneficial to the GEM experiment but also to its competing SDC experiment at SSC, as well as to a larger class of HEP projects (including those at LHC, Fermilab, BNL, Desy, etc.) Moreover, such a general approach could be extended to open the door to big progress in other fields, such as solving problems of inefficiency in PET medical imaging devices. Luckily, the author’s supervisors at SSC had an open mind to science not limited to merely solving the problem of the GEM experiment, but let him work with a broader scope, letting him work with “a mind thinking from outside the box,” which eventually generated a product beneficial not just to all HEP experiments, but to other scientific fields.

The author’s work on such high-performance systems was presented to the scientific community in 1992 at two international conferences, first in Annecy, France (September 21-25 1992) [38] and then in Corpus Christi, Texas (September 29-October 2, 1992) [39], where different ideas [43], [44], [45], [46] and approaches to the implementation of fast, efficient trigger systems were discussed. The author’s proposal, thanks to its key innovations described in the next section, was shown to achieve higher performance at a lower cost when compared to traditional approaches used for decades in First-Level Triggers for HEP experiments.

- i. *High-performance system: author’s “thinking outside the box” generated a solution beneficial not only to HEP but to other scientific fields*

The traditional approach in designing the “decision box” unit executing the First-Level Trigger algorithm was to start from whatever information was provided by the detector group, who decided how to assemble the detector, how to couple the detector to the sensors (or transducers e.g. PMT, APD, etc.), how to define the segmentation of the detector in electronic channels, etc. After all these decisions were made, the electronic group would utilize the information provided by the detector, to implement a “decision box”, which was in fact the translation in circuits of the algorithm provided by the physicists and simulation group. The decision box would implement in analog or more recently in digital form the algorithm in a fixed cabled logic, compromising between cost, speed of the electronics, complexity of the algorithm and high input data rate. Typically the designer of such a “decision box” had the dilemma of favoring one requirement to the detriment of another.

The first decision that the designer in the traditional approach had to take in previous and current experiments, and which severely limited the performance of the system, was the cabling between the detector

and the electronics. Such cabling in the traditional system was done to implement a specific algorithm, and in doing so it was limiting not only the system from future upgrades but also the performance. More specifically it is “one-to-many” (one detector electronic channel or trigger tower to many circuits handling the same data). Such fixed cabling, while satisfying the needs for the implementation of a specific algorithm (e.g. 2x2, 3x3, or 4x4, etc.) was limited to a specific experiment and prevented the same experiment from changing the First-Level Trigger algorithm in the future. The subsequent implementation of the algorithm with “cable logic” limited the performance to the speed of the electronics, the rate of the input data and the complexity of the algorithm.

*The author’s key innovations that allow achievement of higher performance at a lower cost compared to the traditional approach are:*

- *To consider the entire system including the detector assembly, the segmentation of the signals from the sensors in electronic channels and the different algorithms desired to be executed, before conceiving a solution and possibly to suggest the best solution (even for details defining detector assembly and segmentation of the electronic channels) that synergized all requirements*
- *To define a matrix of detector channels and to create an equivalent matrix of electronic channels (in the specific case described here, the matrix consists of 3D-Flow processors [19] working in parallel, each with the capability to execute up to 26 operations in a single clock cycle. The instruction set for such a processor should efficiently execute typical operations required by most triggers.)*
- *To make a “one-to-one” connection between a detector channel (carrying all signals within the view angle of the detector channel or “Trigger Tower”) and its corresponding electronic channel in the equivalent matrix (over 10,000 channels in HEP and of the order of 2,000 channels in PET)*
- *To provide the capability in the electronic programmable processor array of a fast, short latency data exchange with neighbors. This allows implementation of different algorithms (2x2, 3x3, 4x3, 5x5, etc.) while also allowing change of the algorithm for the same experiment when required by the analysis of the first data taken or to accommodate future upgrades*
- *To provide the capability of executing a programmable complex algorithm, sustaining a high input data rate, implementing it in a technology independent platform, at a lower cost compared to the traditional approach. This is possible thanks to the feature of a stack made of several layers of electronic 3D-Flow processor array, each with a data register and a bypass-switch placed in between processors at different layers. This in turn allows execution with no interruption of a programmable complex algorithm relevant to different experiments, or to reprogram the algorithm in the same experiment in order to cope with the more stringent requirements of rejecting “noise” when required by accelerator upgrades to a higher luminosity. An intrinsic feature of the system is its technology independence, allowing use of the most cost effective technology at any time.*

ii. *Construction in hardware of author’s innovative approach that proves its feasibility and advantages*

In spite of all recognitions in letters from emeritus scientists in the field [40], from peer reviewed articles, from public scientific reviews (also at Fermi National laboratory in 1993 requested by the SCC Director who was also the Director of Fermi Lab. See Section 10.b.ii), the author received only \$150,000 during the SSC closeout and little funding from Government grants compared to hundreds of millions of dollars received by the scientists who implemented the traditional First-Level Trigger with limited performance and at a higher cost per particle detected. However, in spite of this, the author was able to build in hardware his innovative idea with personal funding and the support of friends, overcoming all the technical problems that were considered insurmountable (such as the connectivity required in the system) as shown in [32].

## 10. Validation of the Discovery

**The discovery is proven by logical arguments in articles, [18], [19], [32], by simulation (see Sections 11, 12 of [2], Appendix of [12], Chapter 13 of [1]), by construction in hardware of the innovative parts built by the author [15] and by experimental results from third parties (i.e. Siemens [41]) that**

**confirm the claims of the author are correct.** Scientific explanations<sup>1</sup> published in 2000 [18], [28] should have induced scientists to reflect on the contradictions pointed out in this article in Figures 3, 4, 5 and should have been sufficient to make scientists realize they had been wrong for decades to believe those who convinced the world that in order to improve PET, only the crystals should be improved. This is because crystals reached an efficiency of over 95% decades ago (such as LSO crystals). In spite of this, **scientists in academia and industry have continued for over 40 years trying to improve crystals and not the other sections such as electronics that were less than 10% efficient.**

The first demonstration of the proof of concept of the author's innovation in the electronics system was presented at the IEEE-NSS-MIC Industrial Exhibition on November 4-10, 2001, in San Diego (CA). At the Industrial Exhibition booth, the author set up the hardware demonstration of circuits, oscilloscope, input/output test boards to show the execution of real-time photon detection algorithms, centered on each electronic channel of the processor array (3x3 "local maxima" with no boundary, Dept Of Interaction –DOI-, etc.) on the 3D-Flow architecture. This system was built using two prototype boards from Altera (each accommodating a Field Programmable Gate Array circuit FPGA EP20K1000), interfaced with two other prototype boards, one to input data from switches and another to display results on LED.

The user could select two sets of input pattern of data (configuration of the input switches) that would simulate two subsequent events received from the detector. The results were displayed on LED showing if a "local maxima" was detected, while signal waveform on the oscilloscope proved the algorithm execution in a given number of steps and at the expected speed.

This constituted the **hardware demonstration of the proof of concept** that the 3D-Flow system architecture was not "flawed", as was claimed by the IEEE-TNS reviewers in 1999, rejecting his [article N14-18](#) [26]. That article was never published by IEEE-TNS in spite of three IEEE reviewers who agreed to publish it and its proof in hardware.

Further reviews not only of the innovative electronics but of the entire three-dimensional Complete Body Screening (3D-CBS) system took place on several occasions. One of those was on July 1, 2003, in Dallas, Texas when an international scientific review was broadcast via web of the author's innovative 3D-CBS technology targeted to early detection. The review panel of scientists and experts in the field evaluated the project and concluded:

*"Crosetto has done an excellent job of implementing his ideas and in designing the electronics, given his limited economic resources. No error or fault could be found with his claims for the expected performance of the 3D-CBS."*

The video of the event with the author's presentation of the 3D-CBS system and the Q&A sessions with the review panel (and interaction with the participant on the web) is available at [www.3d-computing.com](http://www.3d-computing.com), while the complete review panel final report is available at [42].

Another international review that also involved universities such as "La Sapienza", Rome, Italy and UOIT, University of Ontario, Institute of Technology, Toronto, Canada with the participation in person or via web of an international panel of scientists, medical professionals, members of the Superior Council of Health of Italy and industry specialists took place in Rome on June 23, 2008.

The panel examined the author's findings on how to improve, by over 400 times the efficiency of the current PET machine for whole-body examination. The outcome was positive. Reviewers also compiled a questionnaire where they all agreed on the author's claims and recommended funding of the project. The entire over 6 hour event is available on video at [www.crosettofoundation.com](http://www.crosettofoundation.com)

In spite of these innovative 3D-CBS technology positive review outcomes and of the small incremental improvements of current PET by third parties (who first denied and later admitted the author's claims were correct, - further proof that patients could have obtained those benefits ten years ago and could obtain 40,000% PET efficiency improvement in a single step immediately), there still persist inconsistent objections by decision makers to change the direction of cancer research.

The declared primary objective for making decisions about lifesaving technology should be its benefit to mankind. Those engaged in advancing new technologies in the field of medicine claim saving lives to be the primary objective. However, this does not appear to be the case in the decision making process when it does not

<sup>1</sup> Figure 3-4 page 23, [18] (or Figure 3, [32]) showing the ideal vs. actual in-time coincidence detection of current PET and the efficiency improvement solution and Figure 14-1 on page 136, [18] (or Figure 1, [34]) showing where photons are lost in current PET and how to capture more accurately over 400 times the number of photons

adhere to the standards of scientific inquiry. The rationale used by reviewers of grant proposals submitted by the author in recent years seemed to indicate unconcerned with the goal of saving lives, because the reviewers did not support their rejection claims with scientific arguments, but simply repeated the mistaken claim of other scientists that PET could only be improved by upgrading the crystals.

The basis for **JUDGMENT IN SCIENCE is logical reasoning (and ultimately the result of experiment)** and not merely the opinion of a reviewer unsupported by scientific arguments.

**a) *Reversal of opinion of a major PET manufacturer that further validates the discovery***

In November 2002, leaders of Siemens Medical Imaging Division (the President, the Director of PET, the Director of Advanced Research Group and the Director of the Electronics Group), met several times with the author to discuss his claims of improving PET. In response to these claims to dramatically improve PET by use of more economical crystals and improved electronics, along with other components of PET, they very strongly tried to counter the author's claims with many measurements and arguments intended to prove to the author that their electronics and other sections of PET were fine and that **there could not be room for a substantial efficiency improvement**. They said they had already built 31 prototypes believing they had explored all the possibilities of their current technology.

They made many statements during those meetings with the author in 2002 such as:

*"...the detector [at Siemens] is extremely well characterized..., in fact, very accurate test results... We believe that we're making a very appropriate trade-off of light collection and information extraction, AND THAT IT IS NOT LIMITED BY THE ELECTRONICS".*

**However, those statements were retracted in 2007 when Siemens announced on their own web site [23]:**

*"ultra-fast detector electronics significantly improved [by 70%] count rate performance, image quality, signal-to-noise ratio, lesion detectability and patient scanning flexibility." (See testimonials at [www.crosettofoundation.com](http://www.crosettofoundation.com)).*

Ultimately, logical reasoning and experiment prevailed, proving the viability of the author's discovery and advancing science, though incrementally.

However, it is discouraging to note that, in spite of the positive recognition by the scientific and academic world (i.e., from the scientific reviews of July 1, 2003 and June 23, 2008), in spite of numerous testimonials from emeritus reviewers [40], [42] qualified in specific fields related to the implementation of this innovative technology, and in spite of the feasibility of the innovative sections of the technology, first proven by the author and recently, the author's claims also confirmed by experimental results by third parties (i.e. Siemens), in spite of all this, the author's innovative 3D-CBS technology has not been funded and has been completely ignored during the past decade.

This is even more surprising when one realizes that it would have contributed to lower health care cost for individuals, public and private organizations and the government (see Section 15).

**b) *Admission of the merit of the invention by experts from academia in the field of "First-Level Trigger"***

The author asked scientists at CERN and from other research laboratories to analyze the answers received from industry since the publication of his book [18] and their consistency with the best science to benefit mankind. The immediate response after noting Siemens' test results in 2007 that disproved their 2002 statements that their PET efficiency could not be improved substantially, stated that they were incompetent and that the author **should ask scientists working in the First-Level Trigger for HEP experiments who would provide answers consistent with the best science to benefit mankind**. However, after analyzing documents of the author and others on First-Level Trigger and the answers from other scientists, it will be clear that there are other factors that prevented bringing the benefits of the author's innovations to mankind that goes deeper than the superficial answer of "incompetence". In fact, testimonials [40] show that a few scientists understood parts of the author's innovations, but even with that, such obstacles prevented bringing the benefits to the bed of the patient. Those obstacles will become apparent in what follows.

In this regard there is a record of articles, letters and email exchange between the author and scientists, specifically experts in trigger systems, from the top high energy physics experiments in the world, collected during the past sixteen years. The analysis of what the author or other scientists have proposed in articles in 1992 (and in following years) and the **analysis of the answers (or no answers)** received by the author from the

other scientists will allow identification of where the inconsistency with the best science delayed or blocked the benefit of the author's innovations to the public.

- i. *Testimonials at two international conferences in 1992 regarding the innovative author's approach compared to other approaches*

From the 1992 conferences at Annecy [38] and Corpus Christi [39] cited previously and many other conferences follow testimonials about the author's approach in solving the problem of the First-Level Trigger with a **one-to-one connection** between detector channel and electronic channel, with the **NEWS (North-East-West-South) communications** among neighboring electronic channels and with a **bypass-switch and register in between processors** at different layers. All this allows programmability of the First-Level Trigger, **allows coping with high input data rate, allowing** execution of complex real-time algorithms to **efficiently identify "good events" and filter "background noise"** even when LHC luminosity is increased and lowers the cost (compared to the traditional trigger system) by using the most cost-effective technology thanks to its technology-independent approach. The author's new approach has to be compared to the traditional approach of the First-Level Trigger algorithm presented the same year at the same conferences in Annecy [43] and Corpus Christi [44], [45], [46] with **one-to-many connections** between detector channel and electronic channel, with a **fixed cabled-logic implementation** of the algorithm or with a **logic that poses big constraints between the capability to execute a complex real-time algorithm and sustaining a high input data rate**. Unfortunately "good events" will be missed. The current traditional approach had to commission Application Specific Integrated Circuits (ASICs) with no degree of programmability that do not allow any change to the trigger algorithms. Because such a design is not technology independent, it will incur a high cost of Non Recurrent Engineering (NRE) for low volume chips and will not cope with the higher requirements to selectively identify "good events" with an increase of "background noise" when the collider's luminosity is increased. With specific reference to the LHC experiments, the current trigger implementation for phase I of LHC turns out to be rigid and of high cost (e.g. \$15 million just for the material for the CMS First-Level Trigger). Moreover, when the LHC luminosity is increased it will have to be replaced with a trigger system at an even higher cost.

All during these past sixteen years there have been clear statements recognizing the value and the merit of the author's innovations presented at Scientific Conferences and described in 1992 [38], [39].

- ii. *Major scientific review of the author's innovations requested by the SSC General Director*

The Director of the Superconducting Super Collider (also director of Fermi National Laboratory) requested a major public scientific review of the author's innovations relative to a new conceptual approach for the First-Level Trigger. The review was held at the Fermi National Laboratory on December 14, 1993, in presence of hundreds of scientists and experts in the field from CERN, universities and industry. The review panel compiled a written report where they stated: "*The committee finds this project an interesting and unique concept...*" further adding, "*We believe the concept will work for calorimetry.*" "*We see no technical reason why the proposed ASIC processor [3D-Flow] could not be built in approximately one year.*" [In fact, because of limited funding for the processor, Crosetto built it in FPGA (that is an economical version) in less than one year]. "*The general feeling seemed to be that it could be cost competitive.*" (with respect to the overall system cost of other triggers approach for LHC). One comment about the new architecture stated: "*One unknown with this architecture has to do with the added flexibility provided by the programmability of this system. It is hard to crystal ball gaze, however, there was some feelings that given this feature, experimenters would probably think of clever uses not now possible. Better level one triggering will reduce the data rate into level two.*" The review Panel, therefore recommended **assignment of all funds available** during the SSC closeout phase (\$150,000) to support the author and his research for six months "*To complete the current development and leave the project in a state where it could be continued...*" However, to build a First-level Trigger, LHC experiments received hundreds of millions of dollars. So, why after the clear statement validating the merit of the author's innovation and the benefit it would have brought to science was it not funded while other solutions were pursued, in spite of them being clearly more costly and less powerful and clearly not suitable to reject the noise when the luminosity of LHC is increased in 2013 and 2017?

**Some explanations are provided herein by analyzing the answers (or no answers) received recently**, and more can be found in documents accumulated during the past sixteen years. Some excerpts from the answers received during the last four months follow.

iii. *Unsuccessful attempts by IEEE-NSS-MIC General Chairman to obtain from IEEE reviewers their rejection claims supported by scientific arguments*

On May 8, 2008, the author wrote a letter to Uwe Bratzler the General Chairman of the 2008 IEEE Nuclear Science Symposium and Medical Imaging (IEEE-NSS-MIC) Conference inquiring about the reason for submission rejections that were not supported by scientific arguments relative to the author's five articles (submitted to the same conference in 2007). Bratzler immediately telephoned the author encouraging him to resubmit papers to the 2008 IEEE-NSS-MIC Conference and he, as General Chairman would at least guarantee an answer supported by scientific arguments in the event of further rejection from his reviewers. However all five were again rejected in 2008 without scientific reasons provided as promised by Bratzler.

As a follow-up, it was agreed to hold a webcast review on August 26, 2008 and Bratzler followed with this email on July 31, 2008 to the author: ***"...as indicated in one of my earlier emails, the intent of this meeting shall [be] to have (just!) a few experts who are fully familiar with the -technical- subject matter who may then be able to discuss your invention [innovative 3D-CBS technology] and proposal with you on a purely technical basis. ...they should then be able to tell if your proposal may work or not (and if not, why not)..."***

Because Bratzler identified scientists working on the First-Level Trigger as "experts", the author made arrangements to be present on August 26, 2008 at CERN, the one place on earth where the four largest experiments are being conducted with the most stringent First-Level Trigger requirements. He therefore suggested Bratzler invite Wolfgang Enghardt and Sibylle Ziegler, respectively Chairman and Deputy Chairman of the MIC (Medical Imaging) Section of the 2008 IEEE-NSS-MIC Conference to support their rejection of the five articles submitted by the author.

No one contested the author's innovations and claims presented at CERN broadcast from 5:00 PM to 7:30 PM to the world. Not Enghardt nor Ziegler who still had not provided scientific arguments to support their rejection of the author's papers contested the author's claims. The entire webcast event was recorded and is available for those who could not attend on August 26, 2008.

In order to thoroughly implement the desire expressed by Bratzler in his email dated July 31, 2008 reported previously, the following day the author paid a visit to the leaders of the trigger system of the largest HEP experiments in the world costing over a half billion dollars each and to the CERN Director General. To them he presented his innovative architecture built in hardware in 2003 and shown in the schematic drawings, proving how the hardware implementation solved the communication problem believed not to be feasible. Everyone agreed that the author's architecture one-to-one connection, the NEWS communication, the bypass-switch and register between processors and the programmability of the system would have allowed executing the trigger algorithm of all experiments and would have satisfied the more stringent requirements when luminosity is increased at LHC in 2013 and 2017.

iv. *Meeting with CERN CMS experiment Trigger and Data Acquisition Project Manager*

The author met Sergio Cittolin, CMS Experiment Trigger and Data Acquisition Project Manager, who in the past acknowledged in writing the merits and advantages of the author's innovations, said that the collaboration was not interested in those innovations. These days the entire world is watching the CERN LHC and the people who built it, trusting their fairness in using taxpayer money and in making scientific merit prevail to the benefit of mankind rather than business, power, other interests or agendas. Therefore the author was expecting an answer different from "we are not interested" that he could pass on to taxpayers. Following are the answers from the other leaders in the field at CERN, which explain why the opportunity was missed to spend less for the trigger and have a better performance system to find the "good events" and to satisfy future requirements at higher luminosity.

v. *Meeting with CERN CMS Trigger Technical Coordinator*

Next the author met Joao Varela, CMS Trigger Technical Coordinator, Resource Manager who admitted that the author's innovative approach could have executed CMS Trigger algorithm with greater flexibility and coped with the increased luminosity in 2013 and 2017. Looking at the drawings and hardware board implementation of the author's solution, Varela realized that it would have cost much less than the \$15 million for their trigger composed of 100 crates (just accounting for the material, maybe that figure would more than doubled when including travel, salaries, etc.) At the author's question why they adopted in 1995 their rigid "one-to-many" solution based on a cluster ASIC designed sixteen years ago, while the author presented and published his new trigger approach in 1992 [38], [39], Varela at first answered that the author's solution came

too early, than he corrected himself saying that the collaborators (Wesley Smith from Wisconsin) who paid for some of the trigger chose to use whatever they themselves had developed (the cluster ASIC).

vi. *Meeting with CERN CMS First-Level Trigger Project Manager and CMS Tracker Project Manager*

The author met with Wesley Smith, Level-1 Trigger Project Manager, whom he knew from the time of the SSC in 1992. From that time, Smith always focused on a trigger system that was based on the use of his 3x3 cluster finding ASIC. However, at this point, Smith stated that the solution for the future triggers should be built in FPGA and not ASIC and that CMS now needs the information from the Tracker sub-detector in the First-Level Trigger. This implicitly recognizes Smith's mistake over all these past years. During the meeting, the author had the opportunity to show Smith the schematics and the hardware board built in 2003 of his innovative trigger architecture proving that the high density communication did not have a feasibility problem as Smith had claimed.

Also at this time the author believes that Smith, like his colleague Peter Sharp (CMS Tracker Project Manager who also met with the author on August 27, 2008) is wrong in making that statement, because FPGA can work out a solution to a simple trigger requirement such as the one for the HEP Alice experiment that needs only to compare the sum of some signals received from the detector with a threshold, but it cannot work out for a complex First-Level Trigger such as CMS or Atlas experiments. The author provided to Smith and the scientific community very solid scientific arguments in personal emails and also in the paper [47] presented at the 1999 IEEE-NSS-MIC Conference, showing in Figure 6 of that article that communication in his new trigger system was easier to build and more reliable than in Smith's trigger communication system shown in Figure 5 of the same article. However, in spite of the author having demonstrated with the hardware construction of the system that it was feasible, the article still awaits publication because an anonymous IEEE reviewer claimed (without substantiating his claims) the author's system was flawed. During the meeting on August 27, 2008, Smith also admitted that the first limitation of their approach that precluded changing their trigger algorithm was their choice of the one-to-many connections from the detector to the electronics (imposed in order to use his 3x3 cluster finding ASIC), and also admitted that the author's one-to-one connection, NEWS communication, the bypass-switch and register between processor would have provided much higher performance in selecting the "good evens" and in rejecting "noise." **All these limitations could have been avoided if Smith's answers to the author during all past years as well as the rejection of the author's papers had been analyzed for their inconsistency with science to the benefit of mankind.**

vii. *Meeting with the designer of First-Level Trigger for the CERN Alice experiment*

Among the trigger experts, the author also met Hans Muller, who designed the First-Level Trigger for the Alice experiment, and after hearing the requirement for such a trigger (comparing to a threshold the sum of a few signals after subtracting a pedestal), the author agreed that Muller's use of eighty FPGA was a smart and economical solution to the problem.

viii. *Meeting with CERN Atlas experiment First-Level Trigger Project Manager*

The author also met with Nick Ellis, Level-1 Trigger Project Manager for the Atlas LHC experiment who presented a fixed seven step Level-1 Trigger algorithm for LHC experiments [43], [44] at the same conferences (Annecy and Corpus Christi) to counter the programmable, technology independent 3D-Flow trigger system presented by the author [38], [39]. Ellis was surprised to see the schematics and hardware implementation of the author's architecture in a low-cost IBM PC board, acknowledging that a high degree of communication was feasible. He admitted that such a system could implement Atlas Level-1 Trigger algorithm as well as others, including the one satisfying the more demanding requirements when LHC luminosity is increased in 2013 and 2017.

**The author continued his meetings with other project leaders at CERN who explained that the reason (not just in his case, but in many cases) choices were not determined by the best technology or best solution, but by the electronic, detector, or software group leaders of a university or collaboration who put up the money for a subset of a detector of the project. It was pointed out that power and political issues had more weight than technical and scientific issues and, for example, the decision whether to use one connector rather than another was not based on technical features, but on who had more weight in proposing it.**

## ix. Meeting with CERN Director General

Last, the author met with CERN Director General Robert Aymar who agreed that the concept of **one-to-one** connection, the NEWS communication, **the bypass-switch and register** and the schematics and hardware implementation in an IBM PC (or VME as described in [18]) **had merits compared to the one-to-many** connections, the **fixed algorithm** implementation in **cabled logic**, etc., and asked the author to write him a letter stating the differences and providing the references to the several author's articles, in particular to NIM [19] and the two [38], [39] presented at Annecy and Corpus Christi in 1992 before the decision of the LHC trigger was made in 1995. Aymar promised to talk to Nick Ellis, Sergio Cittolin and other leaders of First-Level Trigger projects. He would then let the author know if the author's request to set up a scientific review would be accepted. For this review, all First-Level Trigger project leaders and experts would be invited, together with all scientists opposing the author's innovative approach such as the IEEE reviewers and more recently Enghardt and Ziegler, so that the author could answer directly their objections and their rejection claims could be analyzed. Doubts and difficulties in understanding innovations that still are an obstacle could be removed and Bratzler's objective to get reviewers' rejection claims supported by scientific arguments and why in their opinion the claimed innovations will not work as he expressed in his July 31 email, will be achieved. This would open the door to advance science by satisfying the most demanding application for triggers at the LHC which would lend strength to its application in other fields, specifically the field of Medical Imaging with enormous benefits to patients through early detection of abnormal metabolism thanks to more efficient PET devices. Aymar also pointed out that although the author's trigger is better, the current approach should solve the current trigger requirements of each experiment according to the simulation group who determined the trigger algorithms for different experiments. This might be true; however, the trigger simulation group was limited by the performance of the implementation of the current hardware, and could not even consider what was stated by the panel of reviewers of the author's innovation at Fermilab in 1993: "**given this feature [new 3D-Flow architecture] experimenters would probably think of clever uses not now possible. Better level one triggering will reduce the data rate into level two.**" Not having built the author's more powerful trigger system, one could not compare how less efficient is the current trigger system that is limited in executing complex real-time trigger algorithms.

Although there have been several **actions during the past sixteen years** that prevented the implementation of innovation to promote progress in scientific research and reduction in premature cancer death, there are **two positive actions** that merit underlining: **the first was when the author's leaders at the SSC let him work with "a mind thinking from outside the box" to solve a problem to benefit mankind** and not just a small group (although made of thousands of scientists) of one HEP experiment. **The second** was when **the SSC Director** (also Director of Fermilab), when facing the unknown of the benefits that could bring the author's innovation to mankind, because of the authority of his position "super-parte" he did what was best for the public, that is, **requesting a public scientific review at Fermilab where experts in different fields related to the innovation had to evaluate and support their claims with scientific arguments**. The author passed the exam. Later he proved that what he claimed was correct because he was able to build the system that he conceived. This proved that everyone was right: the decision of the SSC Director to request a public scientific review, the evaluation of the reviewers who stated: "The committee believes there are no major flaws in the conceptual design" and the author who proved himself and everyone else to be right by building the system in hardware and proving its feasibility and proper operation. However, in spite of all these steps in the right direction, humanity still has not received the benefits from the author's innovation because the decision makers had another agenda. It is hoped that the position of the CERN Director General and of CERN, which the entire world would recognize in being among the most competent in recognizing scientific innovation, will just follow in the steps of the Director of the SSC in 1993 by requesting a public scientific review asking the people in the field to listen to the author's claims and either counter them with scientific arguments or support them so as to open the door to progress as was done by the Fermilab panel in 1993.

## 11. Reducing health care costs while saving more lives

The U.S. alone spent \$64 billion in 2003 on cancer treatment [6] (mainly on drugs for late stage cancer treatment) without achieving a substantial reduction in premature cancer death [1].

The words "screening for cancer" do not necessarily have to be synonymous with driving health care costs through the roof. In fact, even with a much reduced budget for early detection, a better result in number of lives saved from premature cancer death is guaranteed with this innovative technology. When early detection is achieved, drug use drops and the cost for post-surgical treatment decreases because it is needed for a shorter

period of time, in particular when the problem is solved mainly by the removal of an early stage cancer with surgery.

***Institutions (governments, health care systems, etc.) use mammogram screening because it is claimed to save lives.*** PET molecular imaging is more sensitive than mammography (which is based on measuring tissue density). Siemens, after improving 70% efficiency of one part of their PET, states on their website: “ultra-fast detector electronics significantly improved count rate performance, image quality, signal-to-noise ratio, lesion detectability and patient scanning flexibility.” The 3D-CBS is over 400 times (or 40,000%) more efficient than current PET and can screen the entire body with a radiation dosage equivalent to a mammogram. ***It begs the question: How many more lives could be saved using the 3D-CBS technology?***

How many lives are saved from premature cancer death by mammography, PSA, PAP smear, current 4,000 PET, etc.? It is necessary to establish clear procedures for evaluating if different research projects or interventions **truly address the social objective of reducing premature cancer death.** Next Section describes a procedure that can verify quantitatively the extent to which the social objective of the reduction of premature cancer death is achieved by each project.

The issue cannot be solved only with simulations which imply assumptions of some parameters that are difficult to guess. Whenever there is an innovation that can be proven to increase the efficiency of current medical imaging devices and safety to the patient, there is far greater responsibility to NOT delay or block the development and testing of such innovations because of the number of lives lost that could potentially be saved, than to block it merely due to the fear of increasing health care spending. (Although in some case the “fear” is psychological because the new procedure or intervention can prove to save more lives at a lower cost per life saved).

**The situation can be analyzed like any other cost/benefit ratio.** Clearly the main beneficiary should be the patient. Companies (pharmaceutical, etc.) with their attention apparently focused now mainly on cancer treatment at an advanced stage will be able to convert much of their activity to early detection, surgical improvements, and drugs for treating cancer at an early stage.

The National Cancer Institute (NCI) claims a reduction in cancer death of 2% per year.

However, analyzing data from the U.S. Census and U.S. CDC, National Vital Statistics, it shows that the number of cancer deaths among a sample of 288 million people in the U.S. in 2003 was 556,700, while for the same population, during the previous year, was about 6,000 more deaths from cancer. This corresponds to only a 1.04% cancer death reduction. Thus, dividing the annual cancer treatment cost (\$64 billion) by the 6,000<sup>2</sup> lives saved, the current cost per life saved is about \$10.5 million, while with the author’s innovative 3D-CBS solution targeted to early detection it is possible to reduce this cost by a factor of about 40.

The author’s claimed health care cost reduction for cancer is supported by the following using the U.S. as the example:

- **Conservative estimate of the percentage of cancer death reduction through early detection:** Although experimental data show that early detection saves life in 90% to 98% of the cases, in order to have reasonable certainty that goals will be reached, only a conservative estimate of 33% reduction in cancer rate is assumed through screening with a technology that is 40,000% more efficient than current 4,000 PET devices for the purposes of this analysis.
- **Death rate for the age group 50-75 which shows the highest mortality:** Statistical data show an annual percentage for cancer death of 0.5% in the age group 50-75. (300,000 cancer deaths over 60 million people)
- **Number of annual examinations required to save 6,000 lives based on the mortality indicated in item 2 and the estimate of lives saved assumed in item 1:** In order to save 6,000 lives through early detection on a sample of the population showing an annual death rate of 0.5% and using a conservative estimate of 33% success, it is necessary to examine 3,640,000 people annually (calculated as  $[6,000 * 100/33] = 18,181$  lives saved if 100% success.  $[18,181 * 100/0.5 \text{ mortality}] \sim 3,640,000$  needed exams).
- **Cost to examine 3,640,000 people:** Because the cost of the examination performed with the author’s innovative 3D-CBS technology is \$400, to examine 3,640,000 people will cost \$1.5 billion (plus the cost of surgery and post-surgical procedures)
- **Cost for each additional life saved:** Dividing the total cost of \$1.5 billion by the number of lives saved, the cost per additional life saved is \$0.25 million (plus the cost of surgery and post-surgical procedures)

<sup>2</sup> Although this result of 6,000 lives saved is mainly due to smoking cessation or diet change, and a very small percentage is due to research

- **Possibility (very conservatively) to save over 100,000 lives per year at a cost less than half compared to the current annual expense for cancer treatment:** With the author's discovery it is possible to greatly surpass the current limit of saving only 6,000 lives per year from premature death. By screening a larger sample of 60,000,000 people, it will be possible to save 100,000 per year at a cost of \$24 billion (plus the cost of surgery and post-surgical procedures). See bottom left of Figure 8.

## 12. Verifying Achievement of the Social Objective

It is necessary to establish clear procedures for evaluating if different research projects or interventions **truly address the social objective of reducing premature cancer death**. Only research projects or interventions that can show a substantial reduction in premature cancer death supported by scientific arguments should be taken into consideration.

### a) *Defining a procedure that will promote funding of projects that provide greater reduction of premature cancer death*

All projects should first estimate and then experimentally verify the impact of the proposed solution on a representative sample of **10,000 people age 50-75**, selected from a population in a location with a constant cancer death rate of 50 deaths per year recorded over the previous 20 years.

Initial funding should be assigned by evaluating not the number of articles published by the applicant but based on the following five parameters:

1. Cost of the project (per experiment as described above)
2. Number of estimated lives saved (among the sample of 10,000 and when extended to a larger population)
3. Estimated cost for each additional life saved
4. Estimated time to achieve the claimed results
5. How well supported, with solid scientific arguments, are the project or intervention and the above four estimated figures

Funding should be continued for solutions showing actual reduction in premature cancer death as stated in the proposal of the applicant, reduced and eventually stopped for projects that do not meet the declared objectives (after missing several milestones).

During the implementation of the various research phases, **the consistency between social and technical-scientific objectives must not be modified** toward other non-priority objectives. For example, a study showing the discrepancy between the publicly declared social objective of reducing premature cancer death with its technical-scientific implementation into a "Type A PET," prioritized for profit and not for the benefit of the patient is reported in the left column of page 693-694 [35].

When the research project cannot provide significant estimated figures and solid scientific arguments relative to these five parameters, neither in the estimation phase, nor in the experimental phase, this will indicate that the social objective is not a priority and funding should be suspended. Proposals should be tested experimentally keeping in mind that the first absolute requirement is the one that must be safe to the patient (research projects requiring the use of radiation, should comply with a dose less than 100 mrem recommended by ICRP) and should have good scientific grounds to potentially greatly improve health care to the patient compared to existing procedures.

### b) *Example of how the procedure should be applied to proposed projects*

Following are a few examples of research projects of which experimental results in the efficacy in reducing premature cancer death could be compared. Each of the following projects has some potential to reduce premature cancer death. By testing experimentally on a sample population, after analyzing the results it will be possible to determine those more effective at achieving minimum cost per life saved.

- Vaccine
- Spiral CT (radioactive dose should be less than 100 mrem)
- Mammography (radioactive dose should be less than 100 mrem)
- MRI

- PSA
- Temperature Maps
- Current PET (radioactive dose should be less than 100 mrem)
- 3D-CBS (radioactive dose should be less than 100 mrem)

At the end of each year a standardized report for all funded interventions should be compared for cost of the intervention for each sample population, how many lives were saved compared to the standardized criteria and the projection of the lives saved for the following year. The projects accumulating better scores in number of lives saved, in lower cost and in more accurate prediction will earn funding priority.

c) ***IEEE General Chairman ' question about which party should pay for experiments needed to resolve differences of opinion among scientists with regard to innovative proposal claims***

The IEEE-NSS-MIC 2008 Conference General Chairman asked the author in correspondence on May 14, 2008 who should pay for an experiment aimed to gather results that would prove either the proposer of a project or a reviewer to be right when there are differences of opinion.

A logical answer to this question is that the reviewers should be more responsible for finding funding if they cannot support their rejection with solid scientific arguments (in many cases a reviewer is an influential scientist who has access to Government Grant funding that is specifically designated resolving issues with potentially great benefits where the reviewer cannot provide irrefutable rejection claims. If not, the reviewer should bring the proposed innovation to the attention of influential people who are decision makers about spending of taxpayer's money).

The proposer has already made the effort to find a solution to a problem. If the reviewer rejects it and later his rejection is found to be in error because the proposer or third parties built the project proving it to be feasible, it is clear that the reviewer was not competent and it was his responsibility to acknowledge it. A reviewer's task is different from a buyer of a product (e.g. a car, a TV, etc.). He must be knowledgeable in the field to understand advantages, progress and benefits using logical reasoning, before data or the product is available. He must be knowledgeable to be able to decide in which direction research must be directed. A buyer's task is much simpler because has just to test if the performance of a product corresponds to what has been declared or what is written on the label. However, someone had to initially decide to develop and produce that product that was better than previous products without having experimental results.

Therefore reviewers have heavy responsibility for rejecting innovative projects if they cannot support their rejection with solid scientific arguments.

Reviewers should be responsible and accountable not only for identifying the solution with most potential of benefits, but also in the event of a mistake of not recognizing one of those that later turn out to be feasible and greatly reducing premature cancer death and cost compared to current procedures. In the event of such an error, those reviewers should be cited as responsible and accountable for having delayed or blocked the progress and benefit to mankind, for the needless death of millions of people who could have been saved at a lower cost per life saved compared to current procedures and, at least, they should be identified as incompetent in the field, so that their opinion will no longer be considered by the decision makers and will prevent further damages to society.

### 13. Overcoming the Obstacle

The key answers to questions posed to the author at seminars about how to overcome the obstacles that for over a decade blocked the funding of all his innovations related to the 3D-CBS technology demand re-examination of the "unreasonable" answers (or no answers) not based on logical reasoning **consistent with declared objectives** received by the author from the institutions (decision makers in academia and government) that were not supported by scientific arguments. Even now, innovations that were blocked for a decade are just beginning to be implemented in small incremental steps when a giant step to implement them all at once is possible.

This fact, on one hand confirms the validity of the author's claims, but on the other hand, because only some innovations are being implemented in incremental steps, it does not permit obtaining all benefits that could be derived from the reduction of the radiation dose administered to the patient and by the detection of the minimal abnormal metabolism, which is essential in obtaining early diagnosis, the one that saves lives.

In order to support the possibility of overcoming these obstacles, the author has pledged to make a donation in the interest of patients of 80% of the income from licensing his patents and he has conceived a FORMULA that demonstrates advantages to all parties involved in the problem of a substantial reduction of premature cancer death.

**14. Donation by the author of the income from licensing his patents plus a guarantee of accounting transparency**

By donating 80% of the income from licensing his 3D-CBS innovative technology patents, with the goal to accelerate the achievement of the full benefits of this innovative technology, the author has the following specific objectives:

1. Build 3D-CBS devices over 400 times more efficient than current PET, safe to the patient for screening selected groups of people at high risk
2. Donate 3D-CBS devices to health care facilities and provide free screening examinations to low income individuals
3. Educate and disseminate scientific information useful to achieving a substantial reduction of premature cancer death

In addition to the donation, he assures transparency in accounting as he did for the \$1 million grants received in the past from the U.S. Government. It is much more important to save millions of lives.

**15. FORMULA that demonstrates advantages to all parties involved**

The formula conceived by the author can be used by anyone who chooses to provide reasonable answers based on logical reasoning consistent with declared objectives to the benefit of mankind, presenting them a useful model for achieving a balance of power among the business sector, the scientific community and the public interest in approaching solutions to cancer and other problems. (See Table II).

Table II FORMULA that ultimately leads to benefits to the patient as all other parties.

Respecting the role of each party	Type of intervention	Guarantee	Advantages to the interested party	Intervention beneficiary
<b>Donors</b> want to contribute to an humanitarian cause	Charitable donation	Transparent accounting shows that donations have been used for the reduction of cancer death	To be known as benefactors of humanity whose contributions save lives	<b>Patient</b>
<b>Financial investors</b> have the responsibility to guarantee profit to their shareholders	Capital investment	Licenses to use the patents protect the investment against the competition	Profit	<b>Patient</b>
<b>Government</b> has the responsibility to improve health care	Planning the future health care that will improve patients' health	Scientific basis of Crosetto's claims which are confirmed by third parties (Siemens)	Reduction of Government funding of cost per life saved from premature cancer death	<b>Patient</b>

The **PUBLIC SCIENTIFIC REVIEW** GUARANTEES THE FOLLOWING EQUATION

$$\{RR * [i * (D + T + S) + j * (I + L + P) + k (G + B + C)]\} = \text{Benefits to the PATIENT}$$

RR = Respective Role

D = Donation	I = Investment	G = Government planning via grants
T = Transparent accounting	L = License to use patents	B = Scientific Basis (Public review)
S = Lives saved	P = Profit	C = Health Care cost reduction

*i, j, k*, are positive (from 0 to 1) weights factors, quantifiable by each party involved that will each contribute to the benefit of the patient. RR is a positive weight factor (from 0 to 1). It is 1 when all parties respect their role.

For meaningful advancements in life-saving technologies to occur, such a power balance is essential to the decision making process. Unfortunately by not providing “reasonable answers” or using “logical reasoning” consistent with declared objectives, the decision makers in the field of medical imaging, while implementing the over 4,000 PET<sup>3</sup> currently used in hospitals have benefitted business at the cost of providing effective improvement of patient health care.

This unique formula optimizes the power of the inter-relationship of business, science and public interest and puts the patient as first priority, rather than prioritizing business to the detriment of the patient, and can satisfy all parties involved in the solution.

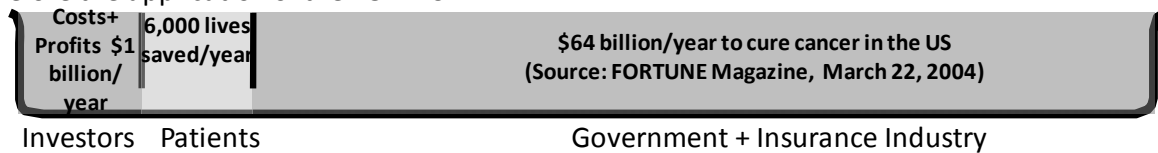
- Donor’s advantage: to be known as a “benefactor of humanity” for a substantial contribution targeted to save many lives from premature cancer death.
- Investor’s advantage:
  - To obtain economic profits from the sale of newly developed equipment with substantially improved efficiency using low cost crystal detectors.
  - To increase production volume, no longer limited by availability of expensive crystals.
- Government’s advantage: to reduce health care cost for each life saved from premature cancer death and receive free 3D-CBS devices (for public facilities) paid for by 80% of the author’s income from patents.

The implementation of the formula foresees that each party is involved in a specific type of intervention applicable to the role of that party and each will obtain the advantages assured by specific guarantees that ultimately lead to benefits to the patient as shown in Table II.

The application of the formula illustrated in Figure 8 shows that thanks to the contribution of the author’s innovation and donation, health care cost is reduced, number of lives saved is increased and market size for these devices is increased (due to increased screening), providing larger profit for investors.

However, although the formula shows potential advantages for each group, to optimize advantages to all of them, it is necessary to respect ethical rules represented in Figure 8 by two vertical separators inside a container that represents the proportion of advantages to all parties involved in the application of the formula.

**Before the application of the FORMULA**



**After the application of the FORMULA**

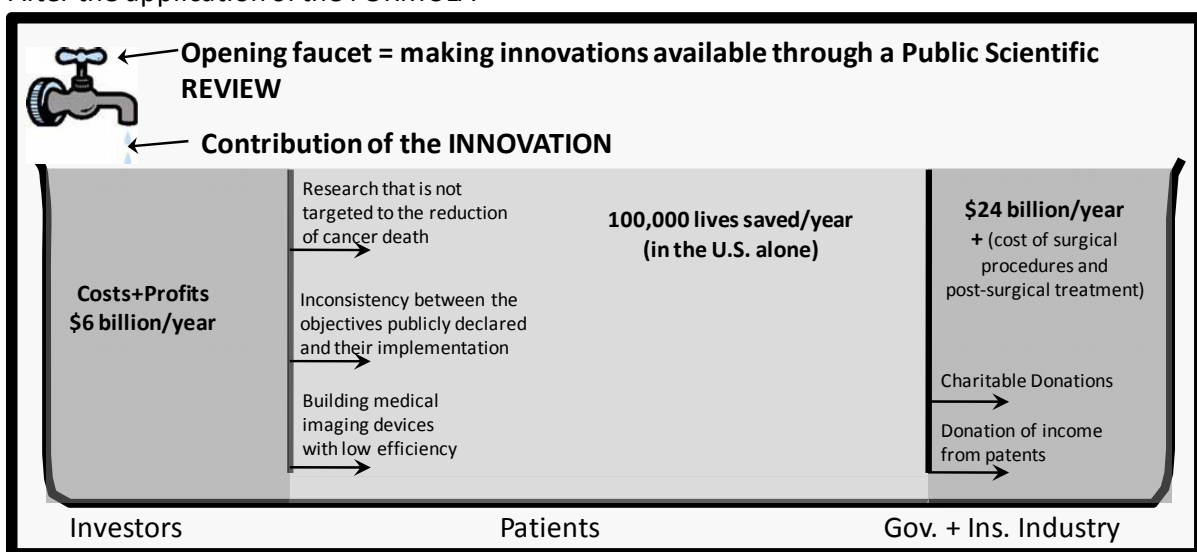


Figure 8 Advantages for all with the implementation of the FORMULA. For investors, the costs + profits are multiplied by 6, for the patients the advantages are multiplied by 16, and for government and the insurance industry costs are cut by more than half. Warning: unethical tampering with the rules will upset the proportional balance of advantages to all parties.

<sup>3</sup> Current PET does not have the capability to detect cancer at an early stage and is not safe to the patient for annual screening due to the high radiation dose required. PET is used mainly to justify the use of expensive drugs.

In fact, unethical tampering with the rules that would increase profit of the investors to the detriment of the patients must be avoided (see in Figure 8 the arrow moving the vertical bar to the right that separates the volume referred to the investors from that of the patients). While on the contrary, the increase of donations causes a reduction in health care cost and an increase of benefits to the patient (see in Figure 8 the arrow moving the vertical bar to the right that separates the volume referred to the patient from that of government and the insurance industry).

## 16. Conclusions

One of the objectives of this paper has been to explain why the author's innovations available for more than a decade have not been supported with their full implementation to benefit scientific research and the reduction of premature cancer death.

The scientists at CERN thought the obstacle was that industry is incompetent and the author should have sought answers from the First-Level Trigger scientists who understand the issues. However, the analysis of approaches published by the author and other scientists during the past sixteen years, the answers received in writing and the testimonial of many scientists points out that choices in the academic and research environment are not fully determined by scientific and technological reasons, but for other reasons which are more typical of a business rather than a research institution.

In "Big Science" it often happens that choices are not determined by the best technology or best solution, but by the electronic, detector, or software group leaders of a university or collaboration who put up the money for a subset of a detector of the project, with the result that power and political issues have more weight than technical and scientific ones.

The response "We are not interested" in a solution to a problem which offers scientific and technological advantages for progress and to mankind is not appropriate from a scientist. It might be from private business, but it is clear that a person working in a research institution that is publicly funded who cannot provide answers consistent with scientific arguments should have to make the choice like the author's former colleagues who, after the closure of the SSC, chose to go to work for a New York Stock Exchange company making up to 35 times the salary received at the SSC.

Analyzing what has been presented in this article should clarify that there are other factors that prevented bringing the benefits of the author's innovations to mankind that go deeper than the superficial answer of "incompetence". Both in industry and in science, the problem is exacerbated by other factors such as politics and outside pressure and not what is in the best interest of the patient or of scientific progress.

The key to get the benefit from innovations is therefore to analyze the answers received from the decision makers and identify the inconsistencies with the objectives so to correct errors and remove misplaced trust from the so called experts who deceive decision makers and the public and take advantage of their position.

The answer is in logical reasoning and reasonable answers that should be consistent across all parties.

Each one should play an important role. Scientists should recognize all innovative proposals, permitting funding for building a prototype with money from taxpayers from donors or from people who have the cause of cancer death reduction at heart, and industry would make them accessible to a large population through production and marketing of medical imaging devices which have all the innovative features implemented at once.

However, the entire world is identifying scientists as the knowledgeable people who can provide a honest opinion if a technology or an approach is better than another for early cancer detection. In these days the entire world is watching the CERN LHC and the people who built it, trusting their fairness in using taxpayer money and in making scientific merit prevail to the benefit of mankind rather than business, power, other interests or agendas. We had **two positive examples** in the past that merit the trust of the taxpayers to the scientific community (see Section 10.b.ix): **the first was when the author's leaders at the SSC let him work with "a mind thinking from outside the box" to solve a problem to benefit mankind** and not just a small group (although made of thousands of scientists) of one HEP experiment. **The second** was when **the SSC Director** (also Director of Fermilab), when facing the unknown of the benefits that could bring the author's innovation to mankind, because of the authority of his position "super-parte" he did what was best for the public, that is, **requesting a public scientific review at Fermilab where experts in different fields related to the innovation had to evaluate and support their claims with scientific arguments.**

Hopefully the leaders in the scientific community will continue to support Science without Secrecy and without Frontiers as stated in the Erice EMFCSC and WFS document and with their support the author will be able to receive rejection claims supported by scientific arguments and he will be able to present his innovations to the ones who are opposing them in a face-to-face scientific review like the one organized by the SSC Director in 1993.

**Because it has been demonstrated scientifically** (with the year 2000 publication of the technical-scientific book “400+ times improved PET efficiency for lower-dose radiation, low-cost cancer screening.”) **that it has been possible to improve** theoretically **the efficiency of the 4,000 current PET** by over 1,000 times (**and practically by 400 times**), because results have shown feasibility and the solidity of Crosetto’s innovations through scientific arguments, through the construction of the hardware of the innovative sections that were proven also by a third party (Siemens), in order not to limit ourselves to more incremental improvements diluted over decades, **it is desirable** that those who have at heart a substantial reduction of premature cancer death (mass media, scientific magazine, conferences, web sites, etc.) **to provide maximum visibility of this article** (and to the material of easier understanding available on the web site [www.crosettofoundation.com](http://www.crosettofoundation.com)) **so that decision makers** who determine the future of health care **will provide reasonable answers, consistent with scientific approaches and the interest of the patient** and as soon as possible **to fund the construction of all innovations of the author**, so not to further delay benefits to the patients.

Finally it is necessary to note that because of the evidence of the scientific arguments presented by the author regarding the whole of his innovations that could already have saved many lives, it is vital that we not find ourselves in the position of having to say in the future: “I am sorry, it **was** possible to increase the efficiency of medical imaging devices ten years ago or more, but... it has not been done” and many people died prematurely needlessly.

In order for each of us to avoid having to give this embarrassing answer, the necessary funding to build ALL these innovations in a single giant step should be made available to the inventor. Only then can we say that each of us has done all that was possible, not being satisfied with an incremental increase of 70% efficiency in one area, but rather getting as close as possible, in a cost effective manner, to the theoretical efficiency (increase of 100,000%).

The author is confident that once a competent analysis of the innovations, accompanied by the formula, is completed, funding will go forward for the improvement of early cancer detection.

What has been highlighted regarding the increase in efficiency that could already have been attained, providing a great reduction in premature cancer death if “reasonable answers” based on logical reasoning consistent with declared objectives had been given, is in fact the “key” to solve other problems, related to simple everyday life, even of planetary dimensions.

## Acknowledgments

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## Glossary

**3D-CBS:** Three-Dimensional Complete Body Screening. Based on Positron Emission Technology measures a dynamic parameter such as minimum abnormal metabolism, blood flow, perfusion, etc. in order to provide accurate information to the physician on any anomalous biological process that can be tagged with a radioisotope. It can be used in Oncology, Cardiology and Neurology. It is mostly known for measuring abnormal metabolism in oncology to provide the physician precious information on glucose consumption by the body cells (e.g. on how aggressive and how fast it is growing) and not merely measuring tumor dimension, although it can provide some information on tumor dimension too. Nevertheless, 3D-CBS provides a more accurate measurement of the tumor dimension because the centroid calculation of the incident photon in the crystal, based on a 3x3 matrix as shown in Figure 6, Section “o”, is more accurate than the 2x2 used in current PET. (By analogy, one is not using a scale to measure how tall a baby is, although most likely we can establish a relationship between the increase in weight and height of a baby. It would be more appropriate to use a scale to measure the weight and a ruler to measure the height. Likewise it is more appropriate to use CT, Ultrasound, X-ray, etc. to measure tumor dimension and the 3D-CBS, or a PET/CT, to measure glucose consumption).

**3D-Flow:** An innovative Parallel-Processing system architecture that allows execution in real-time of a programmable complete algorithm in each processor even if it requires an execution time longer than the time interval between two consecutive input data and allows neighboring (North, East, West, South) data exchange. It is not a hypercube, it is not targeted to execute long general purpose programs, but instead it has an instruction set optimized to execute fast pattern recognition algorithms on pixels of images acquired at high rate, or particle identification algorithms on data acquired at a very high rate from several detectors in High Energy Physics experiments.

The innovative 3D-Flow parallel-processing system architecture was conceived to solve the problem faced in a Trigger system (or “decision box unit”) that should be capable of executing a particle identification algorithm (or First-Level Trigger algorithm or pattern recognition algorithm on pixels of images) on data acquired at a very high rate whose quantity would be impossible to store. If all data from an HEP experiment had to be saved, it would fill up every hard drive on the planet in about one day. The Trigger system has the task of selecting in real-time the highest quality collision events (“good events”) out of many. For example, at LHC it has the task of selecting 100 event/sec out of over 1 million event/second (or about 52 trillion event/day) generated by the machine.

Before the 3D-Flow invention, the problem was solved by creating three or more levels of Trigger. Each level, starting from Level-1 analyzes with increased complexity if the “event candidate” might be a “good event” that will meet all criteria (the three levels of Trigger algorithms) to be accepted and stored on the hard drive. If the “candidate event” fails on some criteria at level 1 or level 2, the process is aborted, data related to the “candidate event” are discharged from the temporary buffer memories to make room for another possible “event candidate” as soon as possible.

Without the 3D-Flow invention, Level-1 trigger has to compromise between: a) complexity of the algorithm that is more or less capable of identifying the desired pattern (or event), b) sustaining an input data rate more or less high and analyzing all pictures (or events) or dropping many of them; c) cost of the electronic system that could be more or less high with a low development cost of low performance electronics or a very high development cost of Application Specific Integrated Circuits (ASIC) with nanometer technology running at GHz executing a fixed algorithm.

Typically the designer of the Level-1 Trigger system (or “decision box unit”) has the dilemma of favoring one requirement to the detriment of another. The invention of the 3D-Flow architecture creates a revolution in the way Triggers can be implemented, eliminating the constraint of designing different Trigger levels (for example Level-1 and Level-2 could be combined increasing the efficiency in capturing more “good candidate events”). The invention of the 3D-Flow architecture overcomes all the above mentioned limitations of current Trigger systems and allows executing a complex and most efficient algorithm in real time to be very selective in discriminating the background noise and identifying even the weak signals carrying the information of the “good event” (or object satisfying the pattern recognition algorithm). It accomplishes this using low-cost off-the-shelf components and technology and it can analyze accurately every picture for the existence of a “good event” (or object satisfying the pattern recognition algorithm) even if the algorithm takes a time for execution that is longer than the time interval between two consecutive pictures.

How is this done? The invention works like a simple game. The first picture “A” goes to a 3D-Flow parallel processing system (layer 1 of processors). The second picture “B” arrives and, because layer 1 is busy, a “bypass switch” forwards it to a register associated with each processor of layer 1 (“Bypass-Register-A”). The third picture “C” arrives, and because layer 1 is still busy, a “bypass switch” forwards it to “Bypass-Register-A”, while picture “B” that was in that register, at the same clock cycle is forwarded by a second ‘bypass switch’ to layer 2 of processors and so on. Processor layers are added in numbers that will allow finishing execution of the algorithm in layer 1 (or in any layer, even if it requires long execution time) even if complex, but that will provide the best chance to identify the desired object (or “good event”). In the event a physicist would like to increase the complexity of the algorithm because he trusts it will be more selective, then one layer (or more) is added to the system. In the event the data rate or the “luminosity at LHC” is increased providing more data, but also more noise and a more selective (complex) First-Level Trigger algorithm is needed, then one layer (or more) can be added to the system.

The beauty of this innovative 3D-Flow architecture is that it is not necessary to use the most expensive leading-edge technology (e.g. an expensive 40 nanometer, GHz technology), but the most cost-effective technology, even at low speed can solve the problem. Thus the innovative 3D-Flow system is technology-independent. When using a low cost, lower performance technology, one just needs a few more layers of 3D-Flow processors. However, if the volume of the 3D-Flow programmable processors increases to justify the development cost (not just of a “Hard Copy FPGA-Altera” process of a few hundred thousand dollars, but that of a “Gate Array” process, or that of a more expensive “Standard Cell” process, or that of even a more expensive development of several masks costing a million dollars in a “Full Custom” process), then the most cost-effective solution that considers the total cost of the system (cost of the development, plus cost of the component) will be chosen. In the latter case of a higher performance technology, the number of layers of

processors needed to execute the same algorithm will be fewer because each processor, running faster, can accomplish more algorithm steps.

**ANALOGY I:** By analogy, it is like having a special movie camera that records only special events that acquire not just 24 frames per second, but 40 million frames per second, and, you need to analyze each frame to check for a specific pattern or object because it is not possible to save 40 million frames per second. Because you cannot record all pictures at that rate, you need a fast “pattern recognition unit” that acquires and processes in real-time all frames at 40 MHz and records only the best candidates that may match your desired pattern or object.

**ANALOGY II:** Let's look at another analogy. Suppose you need to find a pattern in pictures that a team of experts can assess in one hour. However, one picture arrives every minute.

A simple way to understand the 3D-Flow solution is to think of a corridor with 60 rooms along one side. In each room there is a team of experts and a clerk at the door who either passes a picture to the team which he receives from a box on his left, or, if the team is already busy, simply puts it into the box on his right. After one hour of work, the clerk puts the team's result in the right box and gets a new picture from the left one. The system is self synchronized. The very first picture is analyzed by the first team, the second picture by the second team and so on until the 60th picture is analyzed in the last room. When the next picture (61st) arrives in the corridor, the first team has just finished with their analysis and can accept the 61st immediately while their result (yes/no of the first picture) goes down the corridor to the box on his right. The self synchronization of the system makes results flow through the corridor without being analyzed a second time. In that way, only results arrive at the other end of the corridor, one per minute, two hours after the corresponding picture entered the system.

The team of experts in each room is analogous to a 3D-Processor. The clerks at the doors are the bypass switches and the boxes to the right of each room are the bypass-registers.

Notice that the number of rooms containing expert teams must equal the time necessary for the analysis divided by the time interval between pictures. If teams need more time or the input rate of the pictures increases, more rooms can be added at the end of the corridor without changing the conceptual architecture such that the number of rooms still equals the time necessary for analysis divided by the time interval between pictures.

Now that we have a clear idea of a simple system, we can expand our model to the full 3D-Flow architecture.

Since the pictures are very large or complex, we will have to split them into sub-pictures, each to be analyzed by separate teams in parallel who should have access to information neighboring to its sub-picture. To accomplish this, imagine a building with several floors, each with multiple corridors. Work in every corridor is done as above, but the teams will need to communicate with other teams working on parts of the same picture. Each room is connected to the corresponding ones in the corridors in front and behind and above and below (analogous to East-West-North-South). Only the four "near" neighbors are directly connected, but in fact any team working on a part of the same picture can be reached through intermediate rooms.

In High Energy Physics, if your system is not efficient, it will miss the “good events” which means not finding the desired particle, or running the experiment for a longer time (at a high cost).

In medical imaging, this inefficiency for a patient means administering unnecessary additional radiation, small tumors being missed, and only finding those that are too large and advanced to be considered as an early detection – when the greatest chance to save a patient's life is in the past.

**TRIGGER:** decision box unit that should have the capability to selectively recognize within hundreds of nanoseconds, the signals of a “good event” by analyzing a set of many signals arriving from thousands of channels at a very high rate. The Trigger system (or “decision box unit”) must have the capability of executing a particle identification algorithm (or First-Level Trigger algorithm or pattern recognition algorithm on pixels of images) on data acquired at a very high rate that will be impossible to store. If all data from HEP experiments would be saved, it would fill up every hard drive on the planet in about one day. The Trigger system has the task of selecting in real-time the highest quality collision events (“good events”) out of many. For example, at LHC it has the task of selecting 100 event/sec out of over 1 million event/second (or about 52 trillion event/day) generated by the machine. (By analogy, it is like trying to identify a small detail that we call “good event” by analyzing the pixels with a pattern recognition in each frame from your movie camera while you are watching it. The difference is that your movie camera runs at 24 frame per second while a HEP experiment runs at 40 million frames per second). Furthermore, because in nature these “good events” occur randomly, the “decision box” must be capable of capturing and processing two (or more) sets of thousands of signals separated anywhere between a few to hundreds of nanoseconds. The more efficient the decision box is

in capturing and measuring very accurately the characteristics of the possible “good events”, the less radiation is needed and the more chances there are to recognize abnormal metabolisms.

## Acronyms

ACS:	American Cancer Society
ALICE:	A Large Ion Collider experiment at CERN LHC
APD:	Avalanche Photodiode
ATLAS:	One of the four HEP experiments at CERN LHC
ASIC:	Application Specific Integrated Circuit
BGO:	Bismuth Germanate crystal
BNL:	Brookhaven National Laboratory
CDC:	Centers for Disease Control and Prevention
CDF:	Collider Detector at Fermilab
CERN:	European Center for Particle Physics
CMS:	Compact Muon Solenoid experiment at CERN LHC
CT:	Computed Tomography
DESY:	Research Laboratory for Particle Physics – Germany
DOI:	Depth of Interaction
EMFCSC:	Ettore Majorana Foundation Center for Scientific Culture
FDA:	Food and Drugs Administration
FDG:	Fluorodeoxyglucose
FERMILAB:	Fermi National Accelerator Laboratory
FPGA:	Field Programmable Gate Array
FOV:	Field of View
GEM:	Gammas Electrons and Muons Collaboration at SSC
HEP:	High Energy Physics
ICSC:	International Center for Scientific Culture – World Laboratory
IEEE:	Institute of Electrical and Electronics Engineers
KeV:	Kilo electron volt
LIF:	Light-Induced Fluorescence spectroscopy
LHC:	Large Hadron Collider at CERN
LHCb:	Large Hadron Collider Beauty experiment at CERN LHC
LOR:	Line of Response
LSO:	Lutetium Oxyorthosilicate crystal
MIC:	Medical Imaging Conference
MRI:	Magnetic Resonance Imaging
NCI:	National Cancer Institute
NRE:	Non Recurrent Engineering
NSS:	Nuclear Science Symposium
PAP Smear:	Papanicolaou test (checks for changes in the cells of cervix)
PET:	Positron Emission Tomography. (From Greek: Tomography = cuts, or slices of images of the body)
PMT:	Photomultiplier (Transducers converting light into electrical signal)
PSA:	Prostate Specific Antigen
SDC:	Solenoidal Detector Collaboration at SSC
SPECT:	Single Photon Emission Computed Tomography
SSC:	Superconducting Super Collider - Texas
TIR:	Thermal Infrared;
VME:	Computer bus and cards standard
WFS:	World Federation of Scientists

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