

[This document: "[The Solution](#)" in PDF – [5 minute video for layman](#)]

What is Cancer?

Cancer is a disease characterized by the **mutation of normal body cells** into cancerous cells whose main characteristic is reproducing themselves out of control, increasing in volume to the detriment of neighboring tissues, also invading other distant tissue, transported through the blood vessels (metastasis).

Cells become cancer cells because of damage to DNA. Instead of dying, cancer cells outlive normal cells and keep forming new abnormal cells with the same DNA damage as the first cells. Their shape is different due to a different ratio between nucleus and cytoplasm and their structure is irregular. Because they grow faster, **cancer cells need more nutrient** (up to 70 times more than normal) thus showing an abnormal metabolism.

What causes cancer?

We know many causes of cancer. The main ones are: heritage, chemical products (smoke), virus, bacteria, radiation, etc. However, we do not know all of them and most importantly **we cannot know when cancer starts developing**.

How has the cancer calamity been addressed?

Cancer is a serious [calamity](#) affecting over 40% of the world population during their [life time](#) and over 10% will die [prematurely](#) due to that disease.

In the face of such a calamity that causes more premature deaths annually than any war, and therefore which should be enemy number one, we (the world) are [still losing this battle](#) perhaps because a gigantic strategic error is being made.

During the past half century, although enormous investments have been made (in the United States alone [\\$8 billion/year for research](#) and [\\$64 billion/year, mainly for the cure of late stage cancers](#)), the cancer calamity has been almost exclusively addressed through the study and development of new drugs and therapies targeted to the cure of cancer diagnosed at a late stage. These investments have yielded [meager results](#) in terms of a reduction in cancer deaths of less than 2%.

How should the cancer calamity be addressed?

[Experimental data](#) confirm that **cancer diagnosed at an early stage has 90% to 98% probability of resulting in a life saved**. (Diagnosis at a late stage for lung cancer, the number one killer, shows a [survival rate of less than 10%](#)).

It is therefore necessary to address research toward early cancer detection to achieve the capability of capturing the first signals that show the start of a mutation of normal body cells into cancerous cells rather than to focus almost exclusively on the development of drugs and therapies targeted to the cure of cancer at an advanced stage.

In order to understand **which signals are important to be detected**, it is necessary to know how cancer initially manifests itself.

How does cancer manifest itself?

Cancerous cells differentiate from normal cells through different signals that provide information about their mutation.

Such signals are related to changes in: odor, temperature, tissue density, fluorescence, metabolism, perfusion, etc.

Among all these signals, the one most reliable and useful for early detection and useful for reduction of “false positives” and “false negatives” is the change in metabolism that provides information at the molecular level.

What is the best technique to identify cell mutation (early detection)?

Among all techniques to detect signals generated by body cell mutation into cancerous cells (odor, temperature, etc.), **the technique that provides the best signals is the one [measuring changes in metabolism](#)** at the molecular level (although in multimodality with others). This technique called ‘positron emission technology’ captures and counts in a unit of time the signals from the radioactive tracer placed on the molecule of the nutrient to the body cells. Because cancerous cells take up to 70 times more nutrient with respect to normal cells, positron emission technology allows identification of which cells (or a group of cells) take more nutrient than normal, thus a suspected cancer site. (In comparison, [CT](#), X-ray, mammography and all other devices based on tissue density measurement are much less reliable for early detection because 1 cm³ of tissue consists of about one billion cells, too many to be considered to still be at an early stage. In addition, some types of cancer develop without changing density).

After having verified that positron emission technology provides the best signals, one should also realize that the current over 4,000 Positron Emission Tomography (PET) devices that make use of the principle of operation of positron emission technology, because of their low efficiency, cannot provide early detection because they capture with inaccurate measurements only one signal out of 10,000 from the tumor markers (and they require administering a radioactive dose to the patient that is over ten times higher than the one recommended for screening asymptomatic people by the International Commission for Radiation Protection -ICRP).

In order to achieve true safe early detection, it is therefore necessary to focus on greatly increasing the efficiency of current PET.

The fundamental problem to be solved in order to obtain such improvements is the same as the one already faced in High Energy Physics (HEP) experiments.

Description of the fundamental problem relative to the increase in efficiency

The fundamental problem, relative to the possibility of increasing efficiency, to be solved in Particle Physics was the **impossibility of making accurate measurements on ALL data related to radiation (called events) that arrive at very high data rates from the detector** as the result of millions of collisions between particles generated by accelerators such as the [CERN](#) collider [LHC](#). Accurate measurements are necessary in order to be able to distinguish “good events” from those carrying no useful information that are considered as background noise. For example, [LHC](#) detectors can have something like 600 billion events per second. If all that data were saved for study at a later time, it would fill up every hard drive on the planet in only one day. Hence, because of the need to analyze all of them in real-time, a sophisticated [trigger](#) system was created to analyze, select and save in real-time about one hundred of the highest quality collision events per second (this number of events to be saved is related in [HEP](#) to a parameter called “occupancy” for a specific experiment that is estimated by theoretical physicists, where as in Medical Imaging it is determined by the maximum radiation dose that one can give to a patient).

A similar problem also exists in Medical Imaging. In regard to positron emission technology, it is also necessary to sustain a high input data rate of a million events per second arriving from the patient’s body to which was administered a radiation dose. It is necessary to analyze all of them, in real-time, selecting accurately only the good events generated by the tumor markers and excluding the “[scattered events](#)”, “[randoms](#)”, “[multiple events](#)” and the so called background noise.

In summary the problem to be solved has the two aspects of being able to:

1. Cope with a high input data rate in order to fully use all information carried by the radiation
2. Accurately analyze all signals in order to identify all good events

The two aspects are related to the efficiency of the system in particle detection. **The solution is much more important for Medical Imaging than for Particle Physics.** In Particle Physics, inefficiency only causes a delay and a higher cost in discovering new particles. **Much more serious and damaging is inefficiency in Medical Imaging** devices because not only is there a **higher cost to health care** (ultimately to the patient), but it also **requires administering a higher radiation dose, dangerous to the patient, does not provide the necessary sensitivity to diagnose cancer at an early stage, and is not accurate enough to be able to reduce “[false positives](#)” and “[false negatives](#).”**

The Solution of the fundamental problem: Crosetto’s INVENTION relative to the [Trigger](#)

In 1992, Crosetto presented his innovative [3D-Flow](#) programmable technology to the scientific community at two International Conferences in [Europe](#) and in the [United States](#). His innovative approach was described and compared to other approaches targeted to obtain an efficient [trigger](#). The result of this comparison can be determined by analyzing all scientific articles published in [two books](#) relative to the above mentioned conferences.

In addition to clear advantages in cost, in [breaking](#) the [barrier](#) of executing complex real-time algorithms and in sustaining high input data rate, Crosetto’s technology (because of its characteristics of programmability, technology independence, modularity and scalability of the [3D-Flow](#) system) was the only one capable of solving the problem of the first level trigger for different experiments (including satisfying the most stringent requirement in 2015 due to the future increase of [LHC](#) luminosity), while other approaches were limited to the solution of the specific trigger problem for a single experiment for which it was studied and designed (therefore those other approaches need to be redesigned to cope with the higher luminosity of [LHC](#) and for any other requirement of future experiments). In addition Crosetto’s innovative technology opened a new chapter in Medical Imaging targeted to early cancer detection.

Upon request of the Director of the Superconducting Super Collider (also Director of [FERMILab](#)), a scientific review of Crosetto’s innovative [3D-Flow](#) programmable first-level trigger system was held at Fermi National Laboratory on December 14, 1993, in the presence of hundreds of scientists and experts in the field from [FERMILab](#), [CERN](#), universities and industry. The international review panel compiled a written report stating, “*The committee finds this project an interesting and unique concept...*” adding, “*We believe the concept will work for calorimetry [synonymous with [PET](#) detector].” “*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.*”*

It turns out that the above statement referring to the cost competitiveness aspect of Crosetto invention from the 1993 report was and accurate one, as proven later by facts. For example, the trigger system of one experiment at [LHC \(CMS\)](#) turned out to cost 15 million euro, while the

[3D-Flow](#) programmable solution would have cost much less. The feasibility of the [3D-Flow](#) programmable system was demonstrated by the construction of a modular [board](#) with an estimated production cost in series of only 3,000 euro each. Crosetto's programmable, modular, scalable, technology independent [3D-Flow](#) system built in IBM PC, [VME](#) or larger size boards can satisfy the need not only of [CMS](#) experiment, but of any experiment of any size and of any stringent requirements, even for the higher luminosity at [LCH](#) in the future.

Additionally, regarding cost, the report further states "*The committee was impressed with the work already completed by an essentially one person operation*" This statement in 1993 was further confirmed in the final report by the review panel in 2003 when reviewers realized that in fact in a one person operation, Crosetto designed, built and tested in about ten months with a budget of only \$40,000 (personal savings and help from friends), a modular programmable trigger system suitable for any [HEP](#) experiment and [PET](#) Medical Imaging device. This system worked in the first version built, although it presented the [challenge](#) of connecting over 20,000 contact pins on only 8 layers of an IBM PC size [board](#).

This \$40,000, used for the development of the modular [3D-Flow](#) system implemented by Crosetto has to be compared with the development of several triggers for use in [HEP](#) since 1993, used, even considering just the ones for experiments at [LHC](#). Such costs, which include the cost of material, the cost of twelve workshops on electronics for LHC and the salaries of thousands of physicists, engineers and technicians for more than twelve years beginning in 1995 to develop different trigger systems for LHC, each targeted to a single experiment, not suitable for executing trigger algorithms of other experiments, total hundreds of millions of euro.

The 1993 committee report continues, "...**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 [which] could be replaced by a processor farm. It is possible [that] the farm is the same as used for final event processing before storage"

In a few words, **Crosetto's invention has created a revolution in the [HEP](#) trigger system making the 'Level 1-2-3 Trigger approach' obsolete and has enabled 'early detection' and 'lower radiation' to the patient in Medical Imaging.**

Crosetto's invention was recognized valid and [adopted by scientists](#) of the half billion dollar [GEM](#) experiment at the [SSC](#) (TX) in April 1993.

(This invention, beneficial to Particle Physics and Medical Imaging is explained in simple terms by means of an [analogy](#) described on page 26 of the [article](#) presented at Seminars on Planetary Emergency at the World Laboratory in Erice, Italy on August 23, 2008 and is explained in the [video at this link](#)).

An explanation of the same concept in more technical terms is condensed to one page on page 15 of the [article](#) and [animation](#) presented at the University of Geneva, before many scientists from CERN.

The complete trigger system with the 3D-Flow innovative architecture for High Energy Physics experiments is described in a 45 page article that was accepted for publication by the peer review scientific journal *Nuclear Instruments and Methods in Physics Research* – [Part I](#) and [Part II](#).

The 3D-CBS Solution: Crosetto's additional INVENTIONS related to early cancer detection

Crosetto's invention related to the [Trigger](#) has finally solved the two aspects of an enormous fundamental problem relative to the increase in efficiency, until then considered unsolvable in HEP and in Medical Imaging. Because of that, now it is possible to make use of ALL information received from the radiation.

This invention opened the door to [other inventions](#): some dependent on the original invention and others that are independent inventions.

In the field of Medical Imaging such new inventions relate to different technological aspects: mechanics, detector geometry (elongation of the detector), simplified assembly of the detector, coupling of the detector system to the electronic system, real-time execution of photon identification algorithm, etc.

In greater detail, these innovations relate to five main areas:

1. Increased detector length – longer Field of View (FOV) made possible because of the other innovations that allow the use of more economical crystals without a large increase in cost.
2. Improved and simplified detector assembly.
3. Innovative electronics providing a means of:
 - a) accurate identification of the impact point of all photons including the oblique photons and accurate measurement of their total energy;
 - b) reduction of the initial number of the electronic channels; and
 - c) simplification of the method for identifying in-time coincidences.
4. Capability of executing complex algorithms for photon identification.
5. Innovations in the visualization of the information obtained.

The synergy of all these inventions allows capturing more accurately all possible signals from tumor markers at a lower cost for each signal captured providing the physician more accurate measurements of five parameters that allow reduction of “[false positives](#)”, “[false negatives](#)” and the examination cost and enables early diagnosis.

These five parameters are:

1. Accurate measurement of the [total photon energy](#), using the signals received from 9 electronic channels (rather than 4 as used in current PET), that allows discrimination of “good events” from “[scatter events](#)”.
2. Accurate measurement of the photon arrival time (Time-of-Flight -TOF-) that allows to discriminate “good events” from “[randoms](#)” and “[multiple](#)” events.
3. Accurate measurement of the spatial resolution referred to the ‘[x’ an ‘y’ coordinates](#) (distance in the axial and 90° with respect to the axial direction of the impact of the photon into the surface of the crystal. Centroid calculated based on 3x3 array rather than a 2x2 array as used in current PET)
4. Accurate measurement of the photon [Depth Of Interaction](#) (DOI) which allows elimination of the parallax error.
5. The improved signal-to-noise ratio makes it possible because of the capability to execute complex algorithms in real-time, while sustaining at the same time a high input data rate.

These additional inventions related to Medical Imaging are summarized on page 2 of the article "[3-D Complete Body Screening \(3D-CBS\)](#)" and have been recognized by several international scientific reviews. (See the [video](#) and the [final report](#) by the international scientific review committee held in Dallas (TX) on July 1, 2003. See also [part I](#), [part II](#), [part III](#), [part IV](#) and [part V](#) and the report (signed questionnaire) of the international scientific review held in Rome, Italy on June 23, 2008).

A simple description of Positron Emission Technology is available in a [three page document](#).

The main differences between the 3D-CBS technology, 400 times more efficient with respect to current PET are described in simple terms in [this poster](#).

A summary of the advantages derived from Crosetto’s inventions includes:

1. Accurate detection of minimum abnormal metabolism that allows early cancer detection
2. Great reduction of the radiation dose to the patient to a level lower than 1 mSv
3. Reduction of the examination cost and of global health care costs

For a more detailed description of all advantages, go to [this link](#)