A simple description of Dario Crosetto's innovative technology called 3D-CBS (Positron Emission Technology) which is a significant evolution of PET (Positron Emission Tomography)

Each of the 3,000 PET devices used today employs a scanning technique in which the analysis of several layers reproduced as pixels, by correlating several of these layers of information, produces a medical diagnosis on one or more body organs. The technology developed by Crosetto allows instead generation of a medical diagnosis on all body organs simultaneously in three-dimension on the entire body in a single acquisition of voxels[1] data, or screening.

Positron Emission Technology is a technique which shows abnormal metabolism of body cells through the use of positron emission of certain radionucleides. The positron emitted by the radionucleide collides with an electron generating two photons that are emitted in opposite directions. These radionucleides are produced in a cyclotron and are used to label compounds of biological interest. For example, these compounds of biological interest can be the normal nutrient of body cells, such as glucose, oxygen or ammonia, etc. The labeled compound is usually intravenously injected into the body and is distributed in tissues and organs activating the metabolic process. Cancer cells, by being hyperactive, require more nutrient (labeled compound) compared to normal tissues (see Figure 1), becoming in this manner a source of an abnormal number of collisions between positrons and electrons emitting in opposite directions two photons that are detected and measured by the 3D-CBS device.

Because the labeled compound is radioactive, and is capable of causing damage to body cells, radioactivity must be minimized. A compromise needs to be made between giving a sufficient radiation dose to see abnormal metabolism and keeping damage to body cells at a minimum with a low radiation dose. The best solution can be achieved if all possible photon pairs are 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 from the device that must capture the maximum number of pairs of photons produced by the lowest possible radiation dose (see Figure 2.)

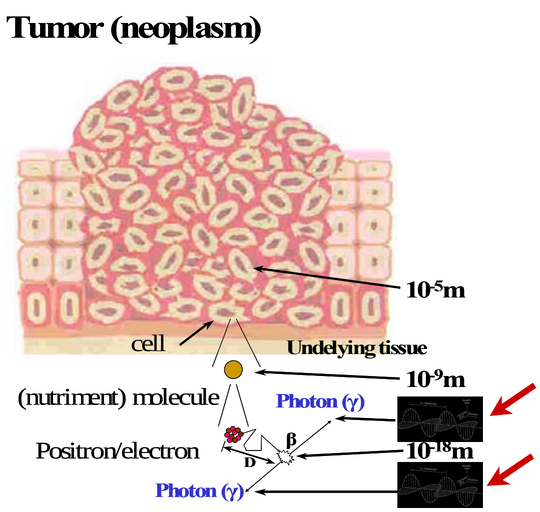

Figure 1. Representation of the cancerous tissue (neoplasm) that must be identified from its natural nutrient uptake (for example: glucose molecules) labeled with a radionucleide. The positron β^+ emitted by the radionucleide, after traveling for a distance D, collides with an electron generating two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

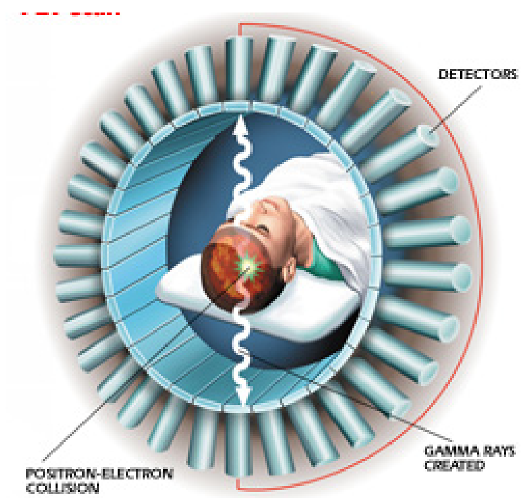

Figure 2. PET detector. Pairs of photons (or gamma rays) hit two locations on the detector virtually at the same time. The intersection of several Lines of Response (LOR) connecting those points reveal the amount of concentration of the radioisotopes (or nutrient to the body cells).

Crosetto's 3D-CBS innovative technology (3-D Complete Body Screening) has the goal of providing information about the smallest abnormal metabolism with the lowest possible radiation dose and cost to the patient. Such an objective is achieved technically when maximum efficiency in detecting pairs of photons is achieved. Because the emission of photons is in all directions, the first action taken in the 3D-CBS project is that of placing detectors in all possible locations around the patient's body in order to cover all organs. In order to contain the

[1] Voxel is a volume element in three-dimensional image array. It is analogous to pixel in a two-dimensional image array.

costs for such coverage, Crosetto uses economical crystals. Compensating for their poorer characteristics he uses an improved, simplified assembly detector (see Figure 3) associated with sophisticated electronics that optimize the measurement of the photon's arrival time, energy, and spatial resolution of the point of impact on the detector. The assembly of the detector in 3D-CBS technology makes use of separations (or cuts) in between crystals filled with reflecting material (or with no cuts) thus allowing light sharing with adjacent sensors (transducers or photomultipliers - PMT's) in all four directions without limitation for the entire surface of the sensor array. The optimization of the measurement of the impact point, the arrival time and the energy of the photons is made possible because of a stack (three-dimensional array) of 3D-Flow microprocessors (see Figure 4). , Each one of the 3D-Flow microprocessors is programmable with an algorithm (or procedure, or simple program) which fully extracts the characteristics of the signal generated by the photon hitting the detector.

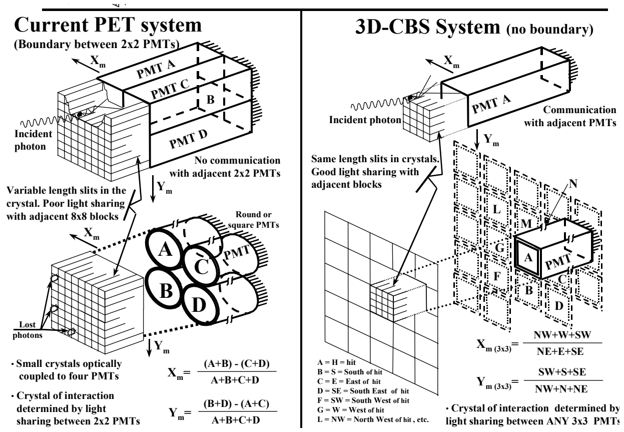

Figure 3. Improved and simplified detector assembly. Comparison between crystal assembly on the 3D-CBS coupled to PMT's that allow an energy center of gravity calculation and the determination of the impact point of the photon with no boundaries (right on the figure) and the assembly of current PET with 2x2 modules (or with fixed segmentation of PMT's) which introduce limitations in the determination of the center of gravity and energy (left on the figure).

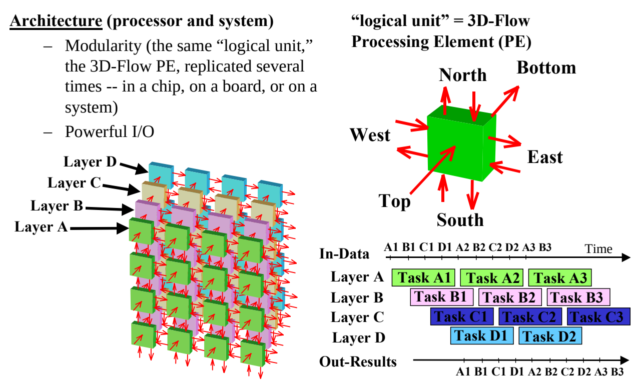

Figure 4. Innovations in the electronics. The stack (or three-dimensional matrix) of 3D-Flow microprocessors allows execution of more accurate algorithms for the measurement of the energy, impact point of the photon. Furthermore the 3D-Flow architecture is technology independent.

The "stack" has two characteristics which are unique in the electronic world that facilitate optimization. Each layer (two-dimensional matrix) of the stack is activated in synchronization. In this manner, each microprocessor can exchange information with adjacent microprocessors in order to calculate precisely the impact point and the energy released by the photon. In particular, it allows precise measurements on the "z" axis of the impact point, thus giving the possibility to capture many more oblique photons at a greater angle that are currently lost in current PET. It can capture approximately the square number of photons compared to current PET which mainly captures photons perpendicular to the axis of the patient. In addition, the number of photons captured is increased by an amount proportional to the square of the length increase of the detector. The solution, never conceived before, to achieve this staggering increase in efficiency is made possible by these inventions that can be implemented in any technology. Either, one can solve the performance need whether it is built with economy, for low volume, at a low speed of 20 MHz, or with an expensive technology for high volume at a few GHz. This is possible because the architecture of Crosetto's system can have depth (the third dimension of the array) which is adjustable in a way enabling all needed time to execute the desired accurate algorithm. When the needed processing time of the algorithm is greater than the time interval between two data acquisitions from the detectors (similar to the interval between taking two pictures), the microprocessors which are busy will forward their information to the successive layer in the stack, until it reaches a free layer. After a cycle of such iterations which is determined by the number of layers in the stack, the first layer that has finished execution of its algorithm, will send the results to the exit of the stack (going through the other layers without further elaborating those results) and will start elaboration on the newly arrived data.

Results obtained from the computation relative to the single photon will be correlated in the electronic system and will determine which one belongs to a possible pair of photons originated by the same collision, which in turn will allow identifying the precise metabolism activity of a specific organ. Besides the need to satisfy the condition of the same arrival time, the pair of photons needs to have the typical energy of the collision process. Photons with energy too far from what is expected might have gone through deviation (scattering) and loss of energy.

1. Technological merits and reduction in cost provided by Crosetto's innovative technology:

- Minimizing the radiation dose used gives a great operational advantage to the 3D-CBS project. The lower dose used in 3D-CBS allows the average time elapsing between single photons (or pairs from a collision) of at least ten times the average time elapsed by photons from the same collision, even when slow crystals are used. Because of this great difference, it will be possible to identify "pure" pairs of.
- Because of the flexibility in depth of the stack, the basic 3D-Flow microprocessor can be built in different technologies at different speeds, and controlling the cost.
- The innovations in the simplification of the assembly of the detector shown in Figure 3, associated with innovative electronics shown in Figure 4, allows increase of the length of the detector as shown in the right section of Figure 5, while using economical crystals that will keep the cost of the machine from being exorbitant and will enable a lower examination cost.
- The geometry of the 3D-CBS that can capture pairs of photons coming from different directions (including oblique photons at large angle), allows achievement of sufficient spatial resolution at minimum radiation dose showing abnormal metabolism.
- Another advantage of the 3D-CBS technology is provided by the fact that it is not necessary to keep track of the change in radioisotope activity and in the change in organ activity because, as in current PET, portions of the body are examined at different times. With 3D-CBS, the examination is performed with the body in a single position and with a single data acquisition.

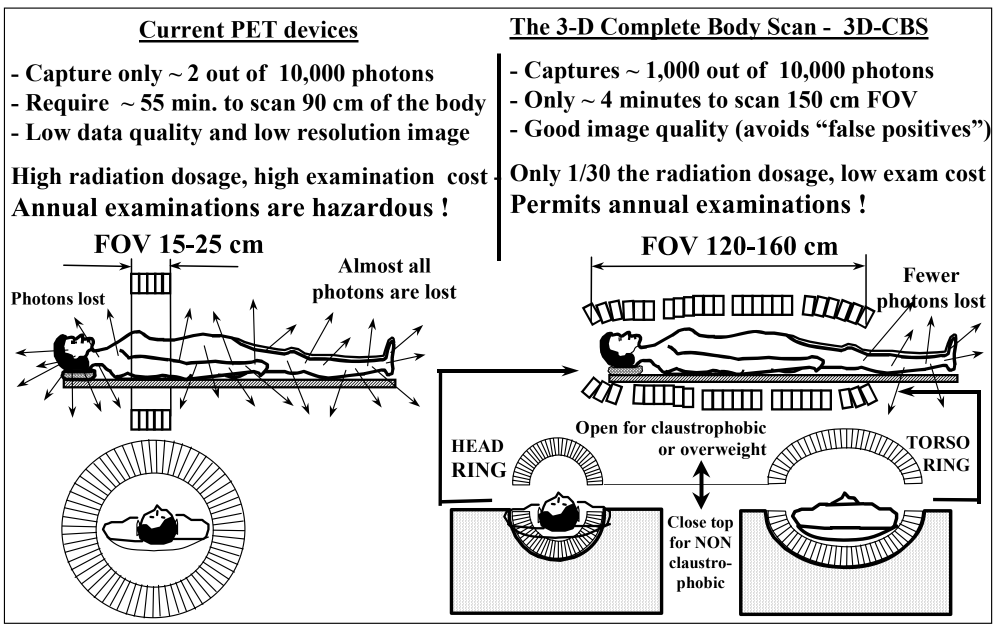

Figure 5. Differences between current PET and the 3-D Complete Body Screening (3D-CBS) as a consequence of the increase of the Field of View (FOV). The increase of the length of the detector in a cost effective manner is possible because of the innovations described in Figures 3 and 4.

2. The most important merits with highest social impact are provided by these innovations:

These innovations have begun a revolution (in terms of benefits in opening new fields of research because for the first time we will have data relative to biological processes, simultaneously, over the entire body and it will be possible to reduce the radiation dose to the patient to a level acceptable by the Commission for Radiation Protection. With detection of the very first cancerous cells due to higher sensitivity, cancer death will be reduced substantially when this examination is extended annually to asymptomatic people at high risk (people with relatives with history of cancer, elderly people, heavy smokers, and people living in high risk environments). These innovations will allow building medical imaging devices similar to the 3D-CBS with economical crystals and sophisticated electronics. This will stimulate competition and reduce costs (to patients, health care providers, governments, insurance companies, etc.)., Following scientific procedures, government agencies should study in depth the benefits provided by this innovative technology and provide research funding to implement all Crosetto's innovations immediately. Everyone should question private industry in this field that does not want to get away from a program that implements incremental improvements assuring profits for a longer time and toward a program that would lower costs.