

La Fisica Medica nell'INFN Massimo Carpinelli

Commissione Scientifica Nazionale 5

- I'INFN ha una lunga tradizione di ricerca nella Fisica Applicata alla Medicina
- La ricerca interdisciplinare nell'INFN viene finanziata principalmente attraverso la CSN5
- Circa 2/3 della fisica interdisciplinare è legata alla Fisica Medica



Summary 2011

FTE	607
Heads	1204
Publications	361
Pubb/FTE	0.59
<if></if>	1.72
<prop.infn></prop.infn>	0.57
Talks at Intern. Conf.	361
Milestones' fulfillment	86%

Talks@Intern.Conf.vs.year

361 talks internazionali (no SIF etc.)



CSN5 Budget and FTE 2012

CSN5 Sector	FTE	Budget (k€)
Detectors, Electronics and Computing	164	1466
Accelerators and Related Technologies	81	753
Interdisciplinary Physics	308	1331

Researc Projects Requirement

- Well defined interest of non INFN institutions (doctors,cultural heritge autorities,etc)
- Ability to attract external funding
- High technology
- INFN expertise well defined and in evidence



Highlights

X-ray Sources Based on Relativistic Thomson Back-Scattering

 $E_x \approx 2\gamma^2 E_{\text{las}} (1 - \cos \Psi)$

Head-on collision: $\Psi = \pi$

 $\lambda_{las} \approx 0.8 \ \mu m$ $\gamma \approx 58 \ (E_{e^-} \approx 29 \ MeV)$ $E_x \approx 20 \ keV$

$$N_X \propto \Sigma_T f \stackrel{e}{e} N_{hv}$$

$$\sigma_{coll}^2$$

 $N_x \approx 10^{10} \gamma/s$



BeaTS



Monday, October 8, 12

SIMULATION

Comparison between monochromatic, quasimonochromatic and conventional X-ray tubes

ICRU Breast Phantom

Thickness: 2-8 cm Details:

Tumor masses and microcalcifications Detector:

amorphous Selenium (0.25mm) Figure of Merit:

$$Q = \frac{SDNR^2}{MGD}$$

Oliva P et al., Med Phys. 36(11) (2009) 5149-61.

RESULTS

Best Energy (keV):

t (cm)	Ideal	aSe	GadOx
2	14-16	14-16	14-16
4	18-22	20-21	18-19
6	22-25	22-23	20-22
8	24-33	27-28	22-25

Quasi mono:

1 keV: Q reduced by < 10% 3 keV: Q reduced by 10-30%

X-ray tube: Q about 60-70% of monochromatic peak Q

Thomson source: Q about 95% of monochromatic peak Q

PHASE CONTRAST IMAGING

• For X-rays at energies of interest for medicine and biology, interacting with biological tissues, the phase shift is generally is generally much more pronounced than absorption. For example, 17 keV X-rays crossing 50 μ m of biological tissue are attenuated less than one per cent, while the phase shift is close to π .

•The registration of this phase shift, together with the absorption, allows to increase significantly the image contrast.

PHASE CONTRAST IMAGING

Spatial variations of the real part of the refraction index cause the wave phase shift, that can be observed by means of the so-called *phase imaging* techniques



n=1-δ-*i*β

β: absorption $(10^{-9} - 10^{-11})^*$ δ: phase shift $(10^{-6} - 10^{-8})^*$ *)biological tissues, for x ray at the 10-100keV range

Brookhaven National Laboratory

Accelerator Test Facility



Dedicated Beam line for Thomson scattering Preliminary Imaging with TS

Phase Contrast?Dual edge imaging?

Phase contrast imaging at the BNL ICS



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Numbers

60-90 MeV e-beam 0.5nC, 30-50µm RMS (50µm to minimize background), 1-3.5ps

CO2 laser, λ =10.6 μm , 0.6 TW, $a_0 \sim$ 0.3 , 5 ps, 30 μm

2 10⁷ x-rays per pulse (>10⁸ x-rays in high background mode) E_x : 6 – 13 keV

WIRE IMAGES

SINGLE SHOT IMAGES

Second run (October 2009)



Single shot, pulse: 4ps. Integration time: 5s.

Oliva P. et al, "Quantitative evaluation of single-shot inline phase contrast imaging using an inverse Compton x-ray source," Applied Physics Letters 97, 134104 (2010)

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IMAGE OF A BIOLOGICAL SAMPLE

SINGLE SHOT IMAGES

Second run (October 2009)



ELIMED

a future Hadrontherapy concept with laser-driven beams





ELIMED Medical Application at the ELI-Beamlines

G A P Cirrone, L Torrisi INFN-LNS, Catania, Italy



Introduction

•Hadrontherapy: one of the most advanced and still pioneering modality in the tumour radiation treatment (40 facilities in operation)

- •Limitation to the hadrontherapy spread: complexity and high cost
- 300 M€, 100 M€ <u>?</u> for the Eye

•The proposed activity related to the study and research of new acceleration techniques and irradiation modalities

- •MoU INFN-ELI
- •Horizon2020 activity ('Best Society' section)

- •Occasion for a common task-force in an unique scientific project involving different INFN competences:
 - Charged particles acceleration and transport (SCENT, MOBIDIC, MC-INFN, Geant4,)
 - Diagnostic of plasma and laser-driven radiation (PLATONE, PLAIA, LIANA-NDT, TRIS, LILIA, UTOPIA)
 - Laser-matter interaction simulation (LILIA,)
 - Hadrontherapy, dosimetry, radiobiology (CATANA, CANDIDO, DORA, PRIMA +,TPS, RDH)

ELI-Beams and the ELIMED idea



• Why ELIMED?

- Realization of a facility at ELI-Beamlines, to demonstrate the clinical applicability of the laser-driven protons
- **Compactness, cost-reduction**, new pioneering treatment modalities



• Why ELIMED at INFN?

med

beamlines

-The project we are proposing is related to the preparatory phase of ELIMED (2013-2015): optimisation of the proton beams, transport, diagnostic dosimetric and radiobiologic studies.



The ELIMED at ELI-Beams in Prague





Expertise in hadrontherapy

30

•CATANA: first Italian protontherapy facility

- p @ 62 MeV by CS for treatment of ocular tumours¹
- More than 330 patients treated
- Tumour local control of 95%²
- Expertise in the development and test of detector for relative and absolute dosimetry

9 4.5

4

3.5 3 2.5 2 1.5

1 Segual

Λ

٥







¹ G. A. P. Cirrone *et al.*, IEEE Transaction on Nuclear Science, Vol. 51, N 3, (2004).

² G. Cuttone *et al.*, THE EUROPEAN PHYSICAL JOURNAL PLUS, vol. 126, 65 (2011)[.]



The laser-driven ion acceleration

Physics principles

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Particle acceleration by high power lasers

•An intense laser field (> 10¹⁸ W/cm²) blows-off electrons from a target surface

•Target Normal Sheath Acceleration or TNSA Regime

•A strong electric field (10 GV/m) is created able to accelerate protons



The possibility of laser acceleration by using intense laser light is very attractive, since the acceleration performance is markedly higher than standard large accelerators and the device size could be much more compact (1/10~1/100) than present facilities in existence.

PRIMA: Proton IMAging

GOAL: Design, construction and test of a proton Computed Tomography (pCT) appartus for medical application in proton therapy centers

FOUNDING

- PRIMA project INFN CSN V
- PRIN2006 project MIUR
- PRIMA+ project INFN CSN V



Research units

- Università degli Studi di Catania
- Università degli Studi di Firenze
 - Dipartimento di Fisiopatologia Clinica
 - Dipartimento di Energetica
- Università degli Studi di Sassari
- INFN, sezione di Cagliari, Catania e di Firenze
- Laboratori Nazionali del Sud-INFN, Catania.





sica Nuclear

Proton imaging motivations

In proton therapy treatments it is important to know:

Patient positioning:

Currently performed using X-rays radiography and tomography in a previous phase

pCT

proton Computed Tomography

allows better accuracy and single phase positioning / treatments

Dose Calculation:

Currently performed using X-rays computed tomography **Problem:**protons and photons have

different interaction with matter



uses protons directly for dose calculation

The pCT apparatus developed is based on "single tracking technique"

Concept

proton Computed Radiography

- Detect the track of the single proton using a silicon telescope
- > Measure the residual energy of the proton using a calorimeter
- Reconstruct the most likely path (MLP) of the single proton
- Calculate the electronic density map

proton Computed Tomography

 pCR for different projections with a rotating gantry

Reconstruct the image





Test at LNS (May 2010): Walnut radiography





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Design of the phantom

First tomographic image (LNS May 2011)

Phantom tomographic images have been reconstructed using the Filtered Back Projection method.

142/256; 256x256 pixels; 32-bit; 64MB



Spatial resolution about 1.5mm

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New iterative algorithms (SART, ART), with MLP reconstruction, are in development and testing phase.

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First tests with high energy proton beam (December 2011 – Uppsala)

pCT prototype installed at the 180MeV proton beam of The Svedberg Laboratory





Data analysis in progress

FUTURE PLANES

- \diamond New reconstruction algorithms development
- $\diamond\, New$ tests with high energy proton beam

Apparatus upgrade: *pCT system for preclinical applications*

- \rightarrow Active area 5 x 20 cm² using the 5x5cm² detectors
- →New data acquisition system





The <u>first ever</u> Italian 7T whole-body MR system for human application is operative at the IMAGO7 Foundation (Pisa).

IMAGO7



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FONDAZIONE STELLA MARIS









IMAGO7



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FONDAZIONE STELLA MARIS ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO



Azienda Ospedaliero Universitaria Pisana



ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO









The first ever Italian 7T whole-body MR system for human application is operative at the IMAGO7





FONDAZIONE STELLA MARIS ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO





Ospedaliero Universitaria Pisana





GRE, TR = 240ms, TE=12.7ms, BW=31.3KHz, FOV 20x20cm, Thkness=4mm, matrix 1024x768, 2 nex

IMAGO7, March 2012

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Radiofrequency coil development for Ultra-High Field magnetic resonance

TESLA (2013-2014)

Technological Equipment and Software for Life-Science Applications)

INFN collaboration:

- Pisa coordinator: Dr. A. Retico
- L'Aquila coordinator: Prof. M. Alecci (Dip. Medicina Clinica, Sanità Pubblica, Scienze della Vita e dell'Ambiente MESVA, Università dell'Aquila)
- Lecce coordinator: Dr. G. De Nunzio (Dip. Matematica e Fisica, Università del Salento)

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SEVEN activity



Several coil models have been designed and developed in Pisa and L'Aquila RF laboratories in 2011-2012 :

- 1. PI Single-loop coils (¹H):
 - simulation and prototype realization for 1.5 T and 7 T MR scanners.
- 1. PI TEM volume resonator for 1H @ 7 T:
 - Collaboration with Jim Tropp (GE senior scientist) for simulations and first prototype realization;
 - 2.a Integrated into the 7 T scanner @UCSF
 - 2.b Integrated into the 7 T scanner @Imago7
- 2. PI Phased array coil for 1H @ 7 T:
 - simulation of the four interacting loops of the phased array;
 - collaboration with Jim Tropp (GE senior scientist) for prototype realization;
 - "attempt" of integration into the 7 T scanner @UCSF (the coil preamplifiers were damaged during the trip).









SEVEN activity

Coils for neuromuscular desease applications

- 4. PI & AQ Dual-tuned surface RF coil (1H and 31P) :
 - simulation of many different coil designs to reach the channel decoupling (4.a, 4.b, 4.c);
 - Final 7 T design (4.d) integrated to the 7 T scanner in Pisa.
- 5. AQ Dual-tuned Microstrip RF coil:
 - the coil was designed, realized and tested at 4 T and 9.4 T MR scanners;
 - the coil design was scaled for the 7 T magnetic field;
 - a coil prototype is integrated into the 7 T scanner in Pisa









INFN

Istituto Nazionale di Fisica Nucleare



In magnet test of the DT-DL coil







σ=0.69 S/m ε_r=79

 1.4×10⁶
 Phantom

 1.2×10⁶
 3¹P spectrum

SPGR image

16-bit;128K

TR=25ms, TE=5.2ms

(256x256 pixels);

FOV=160mmx160 mm

4.0×10⁵ -

2,0×105

AQ: micro-Strip RF coil @7T- 3D CAD & HFSS/CST Model





Tissue

loading

dEA/n

43.8

39.9

37.4 34.9

32.4 29.9

27.4

24.9 22.4

19.9

14.9

12.4 9.87

7.37 4.87 3.00

Dual Tuned (¹H, ³¹P)







- RF coil is a copper microstrip on a substrate composed by 2 PVC slabs (190*105*16*mm^3), with a 29 mm thick air gap in the between and a copper ground plane on the bottom.
- Material properties: PVC: epsilon_r=3.5, Loss_Tang=0.02
- Air gap thickness: 29 mm
- Copper strip dimension: (190*10) mm^2. Thickness 35µm
- Copper ground plane: (190*105) mm²
 Thickness 35 µm
- Capacitance value C1=5.6 pF (capacitors code dG5R6A)

Collaboration UNIV Pisa: Dr.ssa N. Fontana



H field distribution [dBA/m]

@168.6 MHz; y=0 mm (axial)



M. Alecci, SEVEN-AQ

CST

7T DT-microS coil: Assembled prototype

M. Alecci, et al, unpublished results, 2012



Ex vivo pork leg



³¹P Spectrum



Electromagnetic Characterization of MR coil by using Numerical methods

[R. Stara, N. Fontana, G. Tiberi et al, to be submitted]

Many different numerical methods based on the solution c Maxwell's equations can be adopted, e.g.:

- time domain methods, i.e. the Finite-Difference Time-Domain (FDTD),
- frequency domain methods, i.e. the Finite Element Methods (FEM) and the Method of Moments (MoM).

Advantages and drawbacks of these methods are examined while simulating three coil designs:

- 1.5 T proton surface coil;
- 7 T dual tuned surface coil (¹H and ³¹P);
- 7 T proton volume coil.

FEM FIT MoM 7.2pF CT FEM FIT МоМ ____ C₂ См (a) 120pF (b) C4 E field H field 358 MHz 376 MHz SILO-II 401 MHz 419 MHz

Conclusions:
MoM is suitable for simulations at the prototype stage (very fast!)
FEM: similar to MoM, but needs more time.
FIT is suitable to evaluate B₁ and SAR maps once the design has been fixed (it allows simulations with complex humanoid samples; very long execution time!)

WP1. NEW COILS:

- 16-32 ch. Rx Pha Array for knee
- Neck Tx-Rx surface coil
- Volume coil Tx-Rx for small animals



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WP2. SAFETY:

- Electromagnetic Simulations
 - Power deposition in biological tissues (SAR): computation of SAR maps for real-time monitoring at 7T
- New Temperature Sensor:
 - MR compatible prototype for temperature rise monitoring (liquid crystals + fiber optics + readout system)



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WP3. IMAGE PROCESSING and ANALYSIS:

- Postprocessing of 7T image to attenuate inhomogeneities.
- Image segmentation (cartilages, tendons and bones) and quantitative image parameter computation.
- Evaluation of the predictive value of MRI data (psychiatric disorders,
 - neurodegenerative diseases, glioma
 - haracterization) on clinical data (1.5T and
 - T) and feasibility study on 7T data:
 - Structural MRI;
 - Diffusion weighted imaging (tumor segmentation, connectivity maps, ...)

Related abstracts/papers

- R. Stara, N. Fontana, G. Tiberi, M. Tosetti, G. Manara, A. Monorchio, M. Alfonsetti, A. Vitacolonna, A. Galante, M. Alecci, A. Retico, A quantitative comparison of electromagnetic computational methods for RF coil design – ESMRMB 2012, Oct 4-6, Lisbon - accepted abstract.
- G. Tiberi, M. Tosetti, J. Tropp, A. Monorchio, Analytically-Based Approach for the Analysis of MRI Volume Coil Loaded with Multilayered Cylinder, 2012 IEEE International Symposium on Antennas and Propagation and USNC-URSI National Radio Science Meeting, July 8-14, 2012, Chicago, IL, USA.
- R. Stara, M. Costagli, A. Retico, G. Tiberi, M. Alecci, M. Tosetti, *Transverse electromagnetic (TEM) coil for 7T MRI* -Ultrahigh Field Magnetic Resonance: Clinical Needs, Research Promises and Technical Solutions, Berlin, June 8, 2012.
- R. Stara, N. Fontana, A. Monorchio, G. Manara, A. Del Guerra, G. Tiberi, L. Biagi, M. Alfonsetti, A. Galante, A. Vitacolonna, M. Alecci, M. Tosetti, A. Retico, *RF coil design for low and high field MRI: numerical methods and measurements*, IEEE NSS and MIC Conference Records, 2011, 3465 – 3469, Oct. 2011, Valencia, Spain.
- N. Fontana, A. Monorchio, G. Manara, R. Stara, A. Retico, A. Del Guerra, M. Tosetti, G. Tiberi, M. Alfonsetti, A. Galante, A. Vitacolonna, M. Alecci, RF Coil Design: a Comparison of Analytical, Numerical and Experimental Methods for RF Field Mapping, II Congresso Scientifico dell'Associazione Italiana di Risonanza Magnetica in Medicina e dell'Italian Chapter dell'ISMRM, Università di Roma La Sapienza, 31 marzo-1 aprile 2011, page 27.

Theses

- R. Stara, Progettazione e Realizzazione di Bobine a Radiofrequenza per Risonanza Magnetica a Campo Ultra Alto. Tesi Magistrale in Fisica, Università di Pisa. Relatori: A. Retico, M. Tosetti (Ottobre 2011)
- L. Scipioni, Sviluppo di bobine multinucleari per risonanza magnetica a campo ultra alto. Tesi di Laurea Triennale in Fisica, Università di Pisa. Relatore: A. Retico (Giugno 2012)

4D-MPET Giusy Bisogni Università di Pisa e INFN

PET principles







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Since more than 80 years, the PMT is the photodetector of choice to convert scintillation photons into electrical signals in most of the applications related to the radiation detection. This is due to its high gain, low noise and fast response

Research is now moving to solid state photodetectors that show the following advantages with respect to PMTs:

- Compactness
- High quantum efficiency (to provide an energy resolution comparable to PMTs)
- Insensitivity to magnetic fields(PET/MRI)



Avalanche Photodiodes (APDs)

Silicon Photomultipliers(SiPMs) o Geiger-mode APD





-The photon is absorbed and generates an electron/hole pair

-The electron/hole diffuses or drifts to the high-electric field multiplication region

-The drifted charge undergoes impact ionization and causes an avalanche breakdown.

-Resistor in series to quench the avalanche (limited Geiger mode).

As produced at FBK-irst, Trento, Italy



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 \rightarrow High gain \rightarrow Low noise \rightarrow Good proportionality if $N_{photons} << N_{cells}$

The INFN DASiPM2 Project

Progetto SiPM

Sviluppo di rivelatori SiPM

Progetto DASiPM (Development and Application of SiPM)

- Produzione e caratterizzazione di SiPM ottimizzati nella regione 400-500 nm
- Produzione di matrici di SiPM

Progetto DASiPM2 (Development and Application of SiPM)

SiPM Applications:

- Medical Imaging: small animal PET demonstrator
- Astroparticle: TOF SipM module
- High Energy Physics: tracking calorimeter w scintillating fibers



Sezioni di: Bari, Bologna, Pisa, Perugia,Trento



INFN-group V - 2005

INFN-group V - 2006

INFN-group V - 2007

Different geometries



Characterization

Characterization

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Collaboration with FBK- irst (Trento, Italy), that has been developing SiPMs since 2005:

- First detectors Single SiPMs (2006)
- First matrices 2x2 (2007)
- First matrices 4x4 (2008)
- First matrices 8x8 (2009)

Characterization

48

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Vbias (V)



Related to the recharge of the diode capacitance CD from VBD to VBIAS during the avalanche quenching. G=(VBIAS-VB) x CD/q



Dark rate:

- 1-3 MHz at 1-2 photoelectron (p.e.) level, ~kHz at 3-4 p.e (room temperature).
- Not a concern for PET applications.



Intrinsic timing

Intrinsic timing measured at s.p.e level: <u>60 ps (σ) for blue light at 4V overvoltage.</u>

□SiPM illuminated with a pulsed laser with 60 fs pulse width and 12.34 ns period, with less than 100 fs jitter.

Two wavelengths used:

 λ = 400 ± 7 nm and λ = 800 ± 15 nm.

Time difference between contiguous pulses is determined.

The timing decreases with the number of photoelectrons as

□ $1/\sqrt{(Npe)}$ <u>20 ps at 15 photoelectrons</u>.

[G. Collazuol et al., VCI 2007, NIM A 2007, <u>A581</u>, 461-464]



Time resolution



Table 2: Time resolution at 511keV of the tested samples

LSO Ca %	Size (mm ³)	FWHM (ps)	$\sigma \sqrt{2}$ (ps)
0	$2 \times 2 \times 10$	345	104
0.3	$3 \times 3 \times 10$	357	107
0	$4 \times 4 \times 5$	475	143
0.3	$4 \times 4 \times 5$	427	128

Energy resolution



n

Spatial Resolution

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Reconstructed position with center of gravity algorithm. The spatial resolution is about **1 mm FWHM** as obtained with a standard center of gravity algorithm.

Tests of SIPM in a MR system (MRI)

in collaboration with the Wolfson Brain Imaging Center, Cambridge, UK

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S.p.e and ²²Na energy spectra acquired with gradients off (black line) and on (red line).

□<u>No real difference is appreciated in</u> <u>the data.</u>

Differences in photopeak position is due to temperature changes in the magnet

apparent change in gain due to changes in breakdown voltage



[R.C.Hawkes,et al. 2007 IEEE NSS-MIC, Honolulu, USA, October 28-November 3, 2007: M18-118.]

4DMPET Detector module





- 4 Dimensions Module for PET based on a continuous fast scintillating crystal coupled on both sides to arrays of Silicon PhotoMultipliers (SiPM).
- The SiPMs collect the scintillation light providing the impact point, the trigger for the acquisition of the event, the timing and the energy released in the crystal at the pixel level.
- First goal of this project is to achieve a timing resolution as low as 200 ps FWHM to cope with requirements of TOF-in-beam PET dosimetry.
- Depth Of Interaction (DOI) information to improve the spatial resolution of the detector to the ultimate goal of 0.5 mm FWHM in X-Y and of 2 mm FWHM in DOI.
- High integration level, compactness, modularity
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Proposed layout

55

- 4DMPET block detector proposed layout
 - 48 x 48 x 10 mm³ LYSO slab
 - Minimize dead area between blocks
 - 2 SIPM layers 16 x 16 pixel 3 mm pitch ->segmentation
- The signals coming from the arrays of SiPMs are processed by custom Mixed-Mode Front-End ASICs.
 - Each ASIC contains a number of independent channels made up of preamplifier, shaper (filter), discriminators and Time to Digital Converters (TDC)
 - The energy information can be extracted by applying the Time Over Threshold (TOT): the time duration of the signal above threshold can be related to the energy released in the detector
- The Front-End ASICs is controlled by a cluster processor
 - Handles the control signals and the transmission of filtered data to the back-end electronics.
 - Reduces to a minimum the bandwidth required towards the external data acquisition system.
 - Implements on the FPGA cluster processing algorithms such that only cluster position coordinates X, Y, time and TOT are transmitted.

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Front-End Architecture



Time to Digital Converter (TDC)

N. Marino, Uni and INFN Pisa



- <u>fr</u>om the front-end **TOF timestamp:** 100 ps
- TOT timestamp: 400 ps
- □ nominal σ_{LSB} (TOF): 29 ps
- dynamic range: 102.4 ns
- double hit res.: 70 ns
- 26 bit digital output word
- other features:
 - total pulses count
 - * missed event flag

to the cluster processor

Time to Digital Converter (TDC)

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output:

1100110011111000010100000 | flag | TOF | TOT | pulses cnt

илилилилилилилилили

missed even

Ch#



Total simulation time 50+ hours (3 workstation in parallel)

Expected Performances

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 Resolution along x-y RMS 1.6 mm FWHM 0.86 mm FWTM 2.5 mm
Resolution along z RMS 1.7 mm FWHM 1.4 mm FWTM 3.5 mm
Time resolution RMS 660 ps FWHM 170 ps FWTM 600 ps
Energy resolution 10%