TEMPLATE DI PROPOSTA
Call "Research 4 Innovation - 2020"

Generalità, stato dell'arte e Abstract

Nome del progetto:	**Pattern Matching Unit for Medical Application (PUMA)**
Persona Responsabile delle attività:	**Alberto Annovi**
Strutture INFN partecipanti:	**Pisa**
Altri Enti o soggetti coinvolti:	**Fondazione Stella Maris, Elios s.r.l.**
Indicare l'esperimento o altro progetto nell'ambito del quale la tecnologia è stata generata:	**ATLAS**
Indicare progetti in corso o finanziati negli ultimi cinque anni su tematiche analoghe sia all'interno dell'INFN, sia a livello di progetti europei/nazionali/regionali:	FP7-PEOPLE-2012-IAPP FTK (GA N. 324318, international coordinator C. Roda) 254410 FP7-PEOPLE-2009-IOF (Scientist in charge A. Annovi)

Descrizione sintetica del progetto di sviluppo tecnologico proposto
(max 500 caratteri, spazi inclusi).

PUMA can transfer High Energy Physics (HEP) technologies to Magnetic Resonance Fingerprinting (MRF), a new imaging technique based on pattern matching (PM): signal responses for each pixel in the volume are matched to entries from a dictionary of simulated responses. MRF is limited by PM processing time, which scales exponentially with the dictionary size. We developed for HEP a powerful, compact, embedded system, optimized for extremely fast PM. We want to apply it for improved MRF diagnosis.

I. Descrizione della tecnologia

a) Livello di protezione e tutela attualmente applicato (contrassegnare con X). **Nota:** se Software indicare il tipo di licenza applicato (EUPL, GPL, APACHE, etc.)	La tecnologia: - È stata pubblicata (totalmente) X È stata pubblicata (parzialmente) - Sta per essere pubblicata - È o sta per essere brevettata - È stata mantenuta riservata (opzionale) Licenza SW:
b) Livello di maturità attuale della tecnologia	Technology Readiness Level attuale (1-9): 4 for the FTK project technology [3] 3 for the HTT project technology [5]
c) Livello di maturità della tecnologia previsto alla conclusione del progetto (TRL che si vuole raggiungere in relazione all'ambito applicativo individuato nel seguito)	Technology Readiness Level obiettivo (1-9): 7 for the FTK project technology [3] 4 for the HTT project technology [5]

d) Descrivere gli aspetti di originalità e innovatività della tecnologia rispetto allo stato dell'arte. (max 3000 caratteri, spazi inclusi)

In order to complete MRF [0] pattern matching, time evolutions for each image pixel are compared to all the dictionary entries. Each comparison is performed today using a scalar product of measured signals with dictionary elements. The match is observed if the vectors are aligned (maximum value for the scalar product). Scalar products are executed sequentially inside CPUs or GPUs. MRF reconstruction of a typical 3D dataset with 4-5 finely sampled relevant parameters would take a time of the order of days for each performed scan on a high-end workstation [1]. In the clinic, it is important to perform a visual inspection of imaging results within a reasonable time from acquisition. Short reconstruction times are important to translate new MRI protocols from research to the clinical environment. This problem is addressed by using CPUs or GPUs clusters. GPUs accelerate the pattern matching stage of the code. However, because of latency produced from data transfer on the device, GPU acceleration has not exceeded 10x with respect to multi-core CPUs, a factor comparable to the price gap between the devices: the ratio of performance/cost was similar between multi-core CPUs and GPUs. As MRF requires massive parallelism, its algorithm is remarkably similar to the problem of trajectory reconstruction executed in HEP. Our technology has been developed for real time tracking at the CDF first [2] and ATLAS experiment [3] after. It is based on the cooperation of FPGAs and a new, high bandwidth, high density Associative Memory

(AM) ASIC [4]. The AM ASIC is suitable for massive parallelism in data correlation searches and it is the most ingenious piece of the system. It takes full advantage of the intrinsic parallel nature of the combinatorial problem by comparing at once the image under analysis to a set of pre-calculated "expectations", or patterns. The problem is solved by the time data are loaded into the ASIC. Many AM ASICs generations have been developed. The most powerful existing version (65 nm technology), developed for the ATLAS FTK project [3] contains 131072 patterns and is able to execute 10^{14} comparison instructions per sec, working with a 100 MHz clock. Next AM ASIC generation (28 nm) will contain 393216 patterns and will run with a 250 MHz clock. The memory access bandwidth and number of comparisons per second has, to the best of our knowledge, no equal in commercial resources. For MRF applications, we estimate processing time reduction of a factor ~400 for the FTK AM, ~5000 for the HTT one compared to state of the art.

[0] Ma, Dan et al., *Nature* 495.7440 (2013): 187–192. *PMC*. Web. 28 June 2018
[1]G. Buonincontri et al, MRM 2015 doi: 10.1002/mrm.26009
[2]S. Belforte et al. [CDF Collaboration], Nucl. Instrum. Meth. A501:201-206, 2003
[3]S. Citraro et al., IEEE TNS, Volume: 63, Issue: 2 , April 2016, pages 1147 – 1154
[4]M. Dell'Orso, L. Ristori, Nucl. Instrum. Meth. A278:436-440, 1989
[5] ATLAS TDAQ Phase 2 TDR: https://cds.cern.ch/record/2285584

e)

II. Opportunità di mercato

a) I potenziali ambiti applicativi (second use) della tecnologia sono: **Nota**: per *second use* si intendono tutti i settori diversi e ulteriori rispetto a quello della fisica fondamentale.	Elencare tutti i possibili ambiti in cui la tecnologia proposta si può applicare: 1. MRF algorithm acceleration, ~400 times faster than state-of-the-art 2. Edge-enhancing filter for image analysis: data-reduction preserving as possible relevant info, enabling faster data mining. IEEE TNS Vol. 64, Issue 6, June 2017, **Page(s):** 1374 – 1381; this data reduction is relevant to accelerate object recognition. 3. DNA sequencing. 4. Security: identification of specific words into huge flux of sentences.
b) Tra quelli individuati nel punto precedente, selezionare e descrivere nel dettaglio quello che, a vostro parere, è il principale, ovvero quello nel quale la tecnologia proposta esprime le migliori potenzialità in relazione ai vantaggi che conferisce ad un potenziale utilizzatore industriale in termini di minor costo / maggiori prestazioni o benefici rispetto a tecnologie utilizzate a scopi analoghi.	

(max 4000 caratteri, spazi inclusi)

The most important application is MRF acceleration mainly because of two reasons. The first one is that our technology could offer an excellent diagnosis performance improvement with respect the state of the art, with a very large social impact. Our technology compared to the possible use of CPU or GPU farms would save space (much more compact system), energy (lower consumption) and money (lower costs, since we would exploit the R&D development paid by HEP, especially expensive for the ASIC). Historically, quantitative MRI scans have been infeasible in the clinic due to the lengthy scan times to obtain parameters sequentially. The new MRF technique can provide the potential to address this problem by a novel acquisition and reconstruction strategy. Magnetic resonance fingerprinting uses a fast, under sampled acquisition, yielding multiple tissue parameters simultaneously. However, the MRF potentiality is limited by reconstruction time. Short reconstruction times are therefore an important requirement to translate new MRI protocols from the research to the clinical environment. Puma can improve dramatically the performance on under sampled data and the extension of the model underlying MRF to more physiological parameters, such as blood perfusion and water diffusion. Many important advances can be obtained in multi-parametric MRI with the inclusion of further physical and physiological parameters to tackle different aspects of disease without increasing scan time. First, metrics based on diffusion of water are invaluable markers in stroke, cancer, neuron-degeneration and a host of other pathologies. Secondly, new high field scanners have unmasked the effects of magnetic susceptibility changes relevant in neurological diseases such as Parkinson's and Alzheimer's disease and amyotrophic lateral sclerosis (ALS). Features that are highlighted by this mechanism include pathological metallic ion deposits and vascular changes, particularly venous differences, which may be an early warning of pathology at disease onset. In addition, chemical shift imaging can be used to discriminate different contributions to the MR signal, enhancing changes generated by disease and reducing typical image artefacts confounding the exams (such as fat-water chemical shift artefacts). All of these advances, characterized by huge social impact, can theoretically be included in a single three-dimensional acquisition if the processing time problem is resolved.

In addition of these excellent medical perspectives, a second important motivation to prefer the MRF application is our solid collaboration with Fondazione Stella Maris (Pisa, Italy) and GE Health (GEHC at Munich, Germany), excellent institutions, both working on MRF since some years. GEHC is a major scanner manufacturer. It provides the needed expertise and networking to achieve engineering and implementation goals relevant to medical imaging products. The center connects clinical and research needs with development solutions. FSM is a leading center for the study and application of new medical imaging technologies. The center also has a 7T MRI scanner with access to patients with neurodegenerative disease, cancer

as well as psychiatric individuals. Further, the center is located inside a pediatric hospital, and the group has a long and successful history of pediatric research using MRI. This environment will permit the timely application of the techniques developed here to groups of patients with different diseases, with the potential for new discoveries in neurology and radiology.

c) Soggetti cui potenzialmente la tecnologia si rivolge: **Nota:** per "soggetti" si intendono sia i consumatori finali, sia aziende (indicare quali), sia altri enti o istituzioni pubbliche (indicare la categoria).	Elencare tutti i soggetti individuati: 1. – EMC s.r.l., Loc. Drove 14, Centro direzionale Campomaggio – 53036 Poggibonsi (SI), Italy. Interested to board production. 2. – Elios s.r.l., - Via Nicola Pisano 24, 56126 Pisa, PI, Italy. Interested to system integration, validation, commissioning. 3. – FSM interested to system use, performance evaluation. 4. – GEHC for system use, evaluation, dissemination, exploitation. 5. Final consumers: patients needing MRI

d) Enunciare elementi utili a valutare l'impatto economico-sociale della proposta. (max 1000 caratteri, spazi inclusi)

Se possibile completare l'informazione con aspetti quantitativi (ad esempio dimensione del mercato potenziale in quantità di pezzi/anno, possibile scala di diffusione locale/mondiale/nazionale, valore del prodotto finale, etc..).

The MRF technique is a relatively new, highly-promising medical imaging method. Despite this, it has been recognized that the potential for widespread clinical application, as well as the continued development and improvement of the data acquisition, are considerably limited by the low efficiency of reconstruction. By accelerating the MRF algorithm to address this challenge, Puma will increase the MRF capabilities to a clinically-satisfactory level and develop a thorough understanding of this new medical imaging technique. This has the potential of stimulating future European R&D on this topic as well as having a significant impact on the EU healthcare system and economics. At total estimated annual cost of over 3 billion for the European healthcare systems, every percent in reduced MRI scan time or avoided scans (by eliminating unnecessary repetitions) amounts to over €30 million yearly saving.

III. Fattibilità del progetto (compilare foglio excel "Budget R4I - 2020")

Obiettivi del programma di ricerca e sviluppo in termini di avanzamento tecnologico / industriale / di mercato (max 2000 caratteri, spazi inclusi)
(Descrivere gli obiettivi del progetto mettendone in luce la fattibilità e sostenibilità, in relazione alle risorse umane e strumentali disponibili e ai finanziamenti richiesti.)

The Puma goal is the use of one VME board embedding the Associative Memories built for the FTK project [3] for MRF computation: the AM carrier board and the corresponding LAMB Mezzanine plug-in [3]. A single AM-board accessible via network through a VME single board computer can be a powerful MRF accelerator. Our goal is to adapt the exiting software and firmware to make it more general and user friendly and thus ready for intensive interdisciplinary pattern matching execution in the AM ASICs. The project feasibility is based on the partner collaboration, expertise and funds: (a) the hardware (HW) has been provided mainly by INFN funds (CSN1) and ATLAS personnel working in FTK (Annovi, Piendibene, Roda, Giannetti, Liberali, Stabile, Lanza, Negri, Beretta), the EMC company that is in charge for AMboards production; (b) Buonincontri from FSM (MRF expert) will provide the state-of-the-art MRF software and will work with Annovi (AM ASIC expert), Elios company (FPGA expert) to identify and move in the HW the MRF software section to be accelerated. (c) The researcher employed with CTT-FSM funds will develop under the supervision of Annovi and Buonincontri a detailed high-level simulation of the full algorithm to validate the HW through production of precise output expectations to be compared with the HW results.

After the PUMA success, the FTK AM has a natural evolution roadmap in the HTT technology [5] that will allow: (1) better performances (acceleration of factors ~5000) and potentially a smaller system using a PCI express adaptation of PRM mezzanine [5] to minimize the HW size; (2) Cadence license free project or Cadence agreement for the evolution.

The most important goal of the project is the reconstruction of some MRI images with this setup and evaluate the timing performances and the diagnosis accuracy to be compared with the state of the art. This would make the FTK AM ready for usage for MRI imaging.

Indicare in quale modo si pensa che un partner possa sfruttare, con proprie competenze e risorse, la tecnologia nel settore individuato.
(max 1000 caratteri, spazi inclusi)

INFN partners constitute a team that will collaborate to the exploitation of the technology following this plan: (a) FSM is the MRI expert that will profit of the VME prototype (see description below) to perform the first MRI reconstructions, the final goal of this year of activities. The team will decide if VME is friendly enough or a compact version should be produced. (b) GEHC as vendor of MRI instruments will analyze results, will have a determinant role into final decision making and will operate for dissemination; (c) EMC that produced VME HW and is designing the new modern version will be fundamental for HW production; (d) Elios that will participate to software/firmware adaptation and to the first use of the system, will be a key element for commissioning of the system. A friendly HW able to perform very efficient pattern matching can be exploited also for different applications as described in section II. EMC and Elios are candidates to exploit these additional applications.

Indicare l'eventuale coinvolgimento di altri soggetti disposti a partecipare alla ricerca. (max 1000 caratteri, spazi inclusi)

Nota: Indicare eventuale coinvolgimento di:

- Commissioni Scientifiche Nazionali INFN;
- istituzioni esterne e laboratori di ricerca nazionali e/o internazionali;
- industrie, soggetti pubblici o privati;

Nel caso di ente pubblico o privato esterno coinvolto nella ricerca, indicare per ciascuno la tipologia della "background experience", con breve descrizione, e la collocazione nel progetto.

INFN has given a large contribution to the development of the AM technology. Both CSN1 and CSN5 have funded our projects: CSN1 ha funded SVT at CDF [2], FTK and HTT at ATLAS [3,5]. CSN5 has funded an R&D project before FTK and recently (2014) 2 young researchers projects: (a) A. Stabile, Innovative Multi-chip Pattern Recognition Task (IMPART) (b) G. Buonincontri, Quantitative MRI of the Brain Using Magnetic Resonance Fingerprinting MRF: Brain.
In **LPNHE** (Laboratoire de Physique Nucléaire et des Hautes Energies) of Paris F. Crescioli has leaded the AM ASIC design for FTK and is designing now the new version. It is a Mixed Unit of Research (UMR7585) of CNRS, Université Pierre et Marie Curie (UPMC) and Université Paris Diderot, at Campus Jussieu, in the 5th arrondissement. It is composed of 12 research and 5 support groups (administration and services) for a total of about 200 persons. Crescioli is interested to AM applications in the fields mentioned above in section II.

Commentare il foglio Excel "**Budget R4I - 2020**" descrivendo gli aspetti operativi e organizzativi del progetto con particolare riferimento a:

- competenze, ruoli e responsabilità del gruppo di ricerca;
- le attività e le eventuali milestone;
- i deliverable del progetto;
- la richiesta di finanziamento.

(max 3000 caratteri, spazi inclusi)

The expertise of the partners, as already cited, are: (a) INFN personnel is the HW expert; the "pattern matching" technology idea, design, production and exploitation in HEP experiments [2], [3], [5] is due to INFN. (b) the MRF experts are FSM and GEHC: they have a long-standing, effective collaboration translating their development results into MR diagnoses, including quantitative MRF imaging. (c) Elios skills are Real-Time Reconfigurable systems, Computer Vision, Linux, Embedded Graphics. It is specialized in FPGA Design for control, vision and IoT application in all kinds of environments. (d) EMC is an electronic company that collaborated with INFN producing most of the AMboards since its R&D beginning. It is now designing the PRM [5], the last version of AM system for HTT.
The activities are organized into 4 Work Packages (WPs):

WP1: Detailed Simulation of the full MRF algorithm to check the HW. **Leader Buonincontri, FSM**; INFN and Elios collaborate. This WP includes the study of the MRF dictionary to be downloaded in the HW. WP2: HW commissioning. **Leader Annovi, INFN,** EMC and FSM collaborate. The technology and the AM ASIC that is the most innovative device have been proposed for the first time by INFN Pisa, designed and produced by INFN and LPNHE for two HEP experiments [2], [3]. INFN Pisa is the most expert of this technology today. This WP includes the AM bank production/optimization. WP3: MRF algorithm acceleration. **Leader Rossi, Elios**; INFN, EMC and FSM collaborate. This work package includes: (a) the software to connect the algorithm executed in the CPU with the pattern matching executed in the HW; (b) the eventually needed FW adaptations. WP4: Measurement and evaluation of timing and accuracy performances. **Leader Buonincontri, FSM?**; INFN, Elios, EMC, GEHC participate. Deliverables: D.1.1 MRF Dictionary definition and its organization in the AM bank (for pattern matching) ready. M3 D.1.2 Full simulation of MRF algorithm ready. M5 D2.1 VME crate (HW) and AMboard ready for tests. M5 D3.1 Software and FW needed to download data and recover results to/from VME crate, ready for tests. M5 D4.1 Results of a group of MRI reconstructed with new technology; evaluation and comparison with state of the art. M11 D4.2 Dissemination, Exploitation plan. M12 Milestones: M1: HW, SF and FW ready for tests. M5 M2: ~5 MRI images processed with MRF algorithm accelerated by the VME crate. M10 M3: decision between (a) continuation with the VME HW; (b) production of a more friendly setup; M12 Requested funds are 25000 euros totally used to hire personnel: one researcher for the detailed simulation of the whole algorithm (WP1), and a service of 15000 euros for Elios, to work on WP3.

Indicare la presenza di eventuali cofinanziamenti da parte di enti esterni pubblici, industrie, soggetti pubblici o privati:	

ALTRA DOCUMENTAZIONE DA ALLEGARE IN PDF

Documentazione obbligatoria:

- CV (max. due pagine) della Persona Responsabile delle attività e dei Responsabili dei singoli WP.
- Parere positivo dei Direttori o delle Direttrici delle strutture coinvolte per eventuale utilizzo di strumentazione e risorse delle strutture stesse.

Documentazione opzionale/facoltativa:

- Eventuali dichiarazioni di Endorsement da parte di eventuali soggetti esterni,

sottoscritte dalla Persona Responsabile dell'attività delle attività di ricerca collegate alla proposta progettuale.