PhD in Information Technology and Electrical Engineering

Università degli Studi di Napoli Federico II

PhD Student: Emilio Andreozzi

XXXIII Cycle

Training and Research Activities Report – Third Year

Tutor: Prof. Mario Cesarelli – co-Tutor: Prof. Paolo Bifulco

1. Information

I received a M. Sc. Degree, cum laude, in Electronic Engineering from University of Naples Federico II in July 12th 2017 with the thesis "Design and implementation of a device for contactless monitoring of pacemaker activity". I belong to the XXXIII PhD cycle in Information Technology and Electrical Engineering (ITEE), and my fellowship is financed by European PON project funds. My tutors are Prof. Mario Cesarelli and Prof. Paolo Bifulco.

2. Study and Training activities

During my third year of PhD I attended a cycle of seminars organised by g.tec medical engineering GmbH.

a. Seminars
   - BCI & Neurotechnology Spring School - g.tec medical engineering GmbH April 20-24, 2020 (31 hours) [6 ECTS]

	Credits year 3							
		1	2	3	4	5	6	
	Estimated	bimonth	bimonth	bimonth	bimonth	bimonth	bimonth	Summary
Modules	0	0	0	0	0	0	0	0
Seminars	0	0	6	0	0	0	0	6
Research	60	9	3	9	12	9	12	54
	60	9	9	9	12	9	12	60

3. Research activity

- Main research topic:

  Improvements of noise suppression for low-dose X-ray imaging – In my third year of PhD course, my research activity on this topic focused on:

  1) Design and assessment of novel, full-reference, edge-aware IQA index for the quantitative assessment of fluoroscopic sequences quality.
  2) Quantitative performance comparison of derivative operators for fluoroscopy-based intervertebral kinematic analysis
  3) Innovative approach of *a priori* noise characterization for a fluoroscopic device

  First of all, I continued the experimental activity on the performance analysis of NVCA via different image quality assessment (IQA) indices. In particular, during this activity I found that most of the well-established IQA indices tend to disregard the quality degradation that occur on the edges, such as the blurring effects and other kinds of distortion. However, the perception of edges is fundamental for the human vision system to understand the context of the imaged scene, and this is even more important in medical imaging, as the object contours play a key role in diagnosis and in image-guided surgery. To address this issue, I conceived a novel full-reference, edge-aware IQA index, named Sensitivity of Edge Detection (SED), which is based on the assumption that the sharper (and cleaner) are the edges, the better is the edge detection,

which means that the performances of the edge detection can be used as an indirect measure of edges perceptibility. SED considers the edge detection as a pixel classification problem and, therefore, uses the classification sensitivity as a performance parameter. I assessed the performances of SED against two well-established IQA indices, namely the Contrast-to-Noise Ratio (CNR) and the Feature Similarity Index (FSIM), by using synthetic fluoroscopic sequences that I designed with a custom computer program. The sequences were corrupted with simulated Poisson – Gaussian noise and denoised via the NVCA filter, by using several combinations of parameters settings. The preliminary results suggest that SED is more efficient than FSIM and CNR in identifying the denoising results with the highest quality and, therefore, the optimal parameters setting for NVCA that ensures the best trade-off between noise reduction and edge preservation.
The results of this activity where published in the conference paper "*Andreozzi, E., Pirozzi, M. A., Fratini, A., Cesarelli, G., Cesarelli, M.; Bifulco, P. A Novel Image Quality Assessment Index for Edge-Aware Noise Reduction in Low-Dose Fluoroscopy: Preliminary Results. 2020 International Conference on e-Health and Bioengineering (EHB), IASI, 2020, pp. 1-5, https://doi.org/10.1109/EHB50910.2020.9280107*", which I presented at the 8th International Conference on e-Health and Bioengineering (EHB 2020, Iasi, Romania, 29-30 October 2020).

A further experimental activity concerned the application of the NVCA algorithm to the analysis of spine kinematics by means of X-ray fluoroscopy. The automated method for spine kinematics analysis is based on the acquisition of patient spine motion via fluoroscopy and on a template matching approach. The user is first required to select a template of the vertebra to be tracked from a frame of the fluoroscopic sequence; then both the vertical and horizontal image derivatives are computed for the whole sequence and the derivatives of the selected vertebra template are matched in each frame by identifying the linear displacement and the rotation angle that maximize a normalised cross-correlation index. By tracking two adjacent vertebrae, which compose an intervertebral segment, it is possible to analyse the intervertebral kinematics, that is the relative linear and angular displacements between the two vertebrae, as well as the corresponding linear and angular velocities. From these quantities the trajectory of the intervertebral centre of rotation (ICR) can be reconstructed, which has been found to be very sensible to abnormal kinematics observed in several spinal traumas and pathologies. In particular, my research activity focused on the quantitative comparison of the performances obtained by using different derivative operators (Sobel, Prewitt, Roberts and a custom one proposed by Cerciello et al.), which is a rarely addressed issue in the image processing applications based on derivative operators. The performances of the different operators were compared by assessing the differences between their corresponding ICR trajectories via four quantitative parameters: mean and standard deviation of the Euclidean distance between ICR trajectories points, radius and centre-origin distance of the minimum bounding circle of the pointwise difference between ICR trajectories. The results showed that, apart from Sobel and Prewitt operators, which achieved practically identical results, the ICR trajectories obtained by the derivative operators showed detectable differences, which could potentially influence the results of the intervertebral kinematic analysis. Further analysis are foreseen to determine if these differences are effectively relevant for the clinical applications of spine kinematics.
The results of this activity were published in the conference paper "*Andreozzi, E.; Pirozzi, M. A.; Fratini, A.; Cesarelli, G.; Bifulco, P. Quantitative performance comparison of derivative operators for intervertebral kinematics analysis, 2020 IEEE International Symposium on Medical Measurements and Applications (MeMeA), Bari, Italy, 2020, pp. 1-6, https://doi.org/10.1109/MeMeA49120.2020.9137322*", which I presented to the 2020 IEEE

International Symposium on Medical Measurements and Application (MeMeA 2020, Bari, Italy, 1-3 June 2020).

The third experimental activity that I carried out within my main research topic was aimed at conceiving and testing an innovative approach for noise estimation to enable the actual use of the NVCA denoising algorithm in real-time applications on real fluoroscopic devices. Indeed, the NVCA algorithm takes advantage of the *a priori* knowledge of noise statistics to improve its ability to detect and preserve low-contrast edges that are severely affected by quantum noise, thus resulting in substantial improvement of the trade-off between noise reduction and edge preservation in quantum noise suppression. Hence, the availability of accurate noise parameters estimates is essential to ensure the highest denoising performances. The statistics of image noise usually depend on various parameters, e.g. the environmental light conditions, as well as the settings of the imaging device, and for this reason the noise statistics are usually extracted from the raw noisy images to be filtered prior to their processing. However, this could be a problem for many applications, such as the fluoroscopically-guided interventional procedures, which requires the denoising process to be performed in real-time, so as to allow the physician to properly interact with the patient. Considering that in X-ray fluoroscopy the sole light source is the X-ray tube, which is controlled by the fluoroscopic device by acting on the tube current and voltage settings, it could be assumed that quantum noise parameters mainly depend on the selected tube settings. However, they are usually adjusted by the physician to optimize the visibility of specific details, so the noise statistics may vary among distinct fluoroscopic acquisitions and, potentially, even within the same acquisition. This means that, if the noise parameters provided to NVCA have been estimated from a previous fluoroscopic sequence, a mismatch may occur, which could result in a degradation of the denoising performance. It follows that, in order to avoid this event, the noise parameters estimation should be repeated after any change of the X-ray tube settings, but this is hardly feasible in practice. To address this issue, I conceived and tested an approach based on an *a priori* characterization of the noise of the specific fluoroscopic device, which involves the estimation of noise parameters from fluoroscopic sequences acquired at several distinct tube settings. The noise parameters just extracted can be organised in a lookup table, from which they can be retrieved in real-time, by providing the current settings of the X-ray tube, and then fed to the NVCA denoising algorithm. I tested this approach on real fluoroscopic sequences that I had acquired at the laboratories of Technix S.p.A. (Via Enrico Fermi, 45, 24050 Grassobbio, Italy) also with the technical support of General Medical Italia Ltd, by using 5 distinct X-ray tube settings. The results confirmed the feasibility of the proposed approach, which will be extended in future to a larger number of different tube settings, and also highlighted particular relationship between the noise parameters and the corresponding tube settings, which have never been reported before in literature and will be investigated in future works.
This activity led to the preparation and submission of a journal paper, which is currently under revision at the Biomedical Engineering Online journal.

- Other research topics:

<u>*Forcecardiography*</u> – In my third year of PhD course, I carried out further research on this topic, which brought to the discovery of a novel cardiac-related force signal, mainly concentrated in the 0.5-5 Hz band, that seems to be related to the emptying and filling of the heart ventricles. Based on this particular feature, the novel signal could find potential application in the non-

invasive monitoring of the stroke volume variations, which is still an important challenge in cardiology. Essentially, the FSR-based sensor and its conditioning circuit proved capable of measuring, at the same time, the novel force signal related to the ventricles emptying/filling, and a signal very similar to the Seismocardiogram (SCG), which is mainly related to the opening and closing of the heart valves. Considering the heart contraction events as a whole, the overall signal acquired by the FSR-based sensor was named Forcecardiogram (FCG). FCG presents two main components: the Low-Frequency FCG (LF-FCG), i.e. the signal related to the ventricles volume variations, and the High-Frequency FCG (HF-FCG), i.e. the SCG-like signal. The FCG signal was assessed against the ECG signal, as is the benchmark for the monitoring of the heart rhythm. The statistical analyses that were carried out to compare the inter-beat intervals measured via the FCG with those provided by the ECG, confirmed the strong relationship between FCG and the mechanical activity of the beating heart.

This research activity, carried out in collaboration with Prof. Dario Gargiulo of the Western Sydney University, led to the publication of the international patent "*Andreozzi, E.; Esposito, D.; Bifulco, P.; Gargiulo, G.D. Physiological parameter sensing systems and methods. PCT/AU2020/051107. Australian Patent Office. 15/10/2020*", and to the publication of the journal paper: "*Forcecardiography: A Novel Technique to Measure Heart Mechanical Vibrations onto the Chest Wall*" on the journal Sensors (MDPI).

<u>*Federica prosthetic hand*</u> – In my third year of PhD course I joined a research activity concerning the development and performance assessment of the "Federica" prosthetic hand, a low-cost, under-actuated, myo-controlled upper limb prosthesis that uses a single servo motor and a custom differential pulley system, connected by inelastic tendons, to accomplish a fast and effective grasp function. In a first development stage, the Federica hand was controlled via surface Electromyography (sEMG), which requires the acquisition of the electrical activity of a subject's muscle and a further processing to extract the linear envelope of the EMG signal (EMG-LE). However, considering the many drawbacks that EMG presents in the context of long-term muscle monitoring, an alternative control strategy has been investigated, which is based on the Forcemyography (FMG). FMG relies on force sensors that, when placed on a muscle with a proper mechanical coupling, are able to measure the variations of its cross-section area due to the muscle swelling that occur during contraction. In particular, the Federica hand is equipped with the FSR-based sensor I worked on in my previous research, which proved capable of directly providing a signal that is highly correlated to the EMG-LE and allowed replacing the EMG-based control system with FMG-based one. In addition, a novel and simpler conditioning circuit for the FSR-based sensor has been designed based on the well-known current mirror topology. These and other improvements that had been brought to the Federica hand, represent the current state of the art of the prosthesis and were presented in the journal paper "*Esposito, D.; Savino, S.; Andreozzi, E.; Cosenza, C.; Niola, V.; Bifulco,P.: The Federica hand*", which is currently under revision at the journal Research in Biomedical Engineering (Springer).

A further experimental activity was carried out to evaluate the actual grip force exerted by the Federica hand, which is important to evaluate its efficacy and energy efficiency in daily life as well as in more demanding tasks. To this aim, a custom force measurement handle, equipped with a load cell, was designed and assembled. Several measurements were performed by making the Federica hand close to its limit while rotating the handle in different angular positions so as to measure different components of the complex set of forces exerted by the hand. The servo motor current sink was simultaneously monitored, as it is related to the torque and, therefore, to the force exerted on the main prosthesis tendon, which is then transmitted to the fingers via the differential pulley system. By computing the ratio between the force measured by the custom handle and the force indirectly measured via the current sink of the servo motor, it was possible to estimate the force transfer ratio, which quantifies the energy efficiency of the prosthesis. The Federica hand turned out to attain an efficiency much higher and at least comparable to many other well-established upper limb prostheses, apart from those based on hooks, which however do not provide human-like grasping functions.

The results of this activity led to the publication of the journal paper "*Esposito, D.; Savino, S.; Cosenza, C.; Andreozzi, E.; Gargiulo, G.D.; Polley, C.; Cesarelli, G.; D'Addio, G.; Bifulco, P. Evaluation of Grip Force and Energy Efficiency of the "Federica" Hand. Machines 2021, 9, 25. https://doi.org/10.3390/machines9020025*" on the journal Machines (MDPI).

Automated ECoG electrodes recognition in CT volumes – In my third year of PhD course I also joined a research activity aimed at conceiving and testing an automated method for Electrocorticography (ECoG) electrodes recognition in computed tomography (CT) head volumes. ECoG is the most used technique to measure the electrical activity of the brain cortex and is undoubtedly the most widespread tool to monitor the patients affected by drug-resistant epilepsy. The aim of such a methodology is to locate the cortical regions from which the epileptic seizures usually start, commonly referred to as epileptogenic foci. The recognition of these foci is based on the analysis of their local electrical activity. However, once that some of the acquired ECoG signals are recognized as potential epileptogenic foci, they should be accurately located onto the cortex. For this reason, the patients usually undergo a CT scan after the implantation of ECoG electrodes, in order to be able to locate the position of the electrodes that recorded specific brain signals. The ECoG electrodes recognition and localization is performed via computer programs (e.g. iELVIS, ALICE) that still rely on a substantial manual intervention of an expert user, which requires at least one hour to provide the location of the ECoG electrodes within the CT volume of a single patient. To address this issue, an automated method for ECoG electrodes recognition was conceived, which is based on a shape analysis of voxel clusters within the CT volume. In practice, after a first pre-processing stage of the CT volume, a thresholding is performed on the Hounsfield Unit (HU) value of each voxel, in order to identify those with very high HU values, which belong to metal objects. Then, the 6-connected clusters of voxels with HU units above the threshold are located to identify the ECoG electrodes. However, this operation does not allow locating the ECoG electrodes selectively, as indeed other metal objects may be found within the CT volume (e.g. grafts, stiches, wires, screws, metal dental fillings etc.). Therefore, a shape analysis of the voxel clusters is performed by computing 6 distinctive features (volume, principal axes length, circularity and cylinder-similarity) of the ECoG electrodes shapes, which are essentially flattened cylinders (small disks). These features are then fed to a Gaussian Support Vector Machine (G-SVM) to distinguish the actual ECoG electrodes from all other metal objects within the CT volume. The proposed method was tested on a database of 24 patients' CT volumes provided by Neuromed S.p.A. and on a public database from Mayo Foundation for Medical Education and Research, achieving in both cases an unprecedented classification accuracy, that turned to be as high as 99.7 %. Preliminary results also suggested the possibility of using the proposed method to simultaneously detect also the depth electrodes, which are essentially sleeve-shaped electrodes arranged on a thin tip that is inserted in the brain to reach its deepest regions. Indeed, the method attained a classification accuracy in excess of 99 %.

This activity led to the preparation and submission of the journal paper "*Centracchio, J.; Sarno, A.; Esposito, D.; Andreozzi, E.; Pavone, L.; Di Gennaro, G.; Bartolo, M.; Esposito, V.; Morace, R.; Casciato, S.; Bifulco, P.: Efficient Automated Localization of ECoG Electrodes in CT Images Via Shape Analysis*", which is currently under revision at the International Journal of Computer Assisted Radiology and Surgery.

- Collaborations:
  - Western Sydney University, Prof. Gaetano Gargiulo
  - Aston University, Dr. Antonio Fratini
  - Istituti Clinici Scientifici Maugeri, Dott. Pietro Balbi
  - Reykjavik University, Prof. Paolo Gargiulo
  - IMT Atlantique, Dr. Francesco Ferranti

4. Products

a. Journal papers:

- *Andreozzi, E.; Fratini, A.; Esposito, D.; Naik, G.; Polley, C.; Gargiulo, G.D.; Bifulco, P. Forcecardiography: A Novel Technique to Measure Heart Mechanical Vibrations onto the Chest Wall. Sensors 2020, 20, 3885. https://doi.org/10.3390/s20143885*
- *Esposito, D.; Savino, S.; Cosenza, C.; Andreozzi, E.; Gargiulo, G.D.; Polley, C.; Cesarelli, G.; D'Addio, G.; Bifulco, P. Evaluation of Grip Force and Energy Efficiency of the "Federica" Hand. Machines 2021, 9, 25. https://doi.org/10.3390/machines9020025*
- *Andreozzi, E.; Fratini, A.; Esposito, E.; Cesarelli, M.; Bifulco, P. Toward A Priori Noise Characterization for Real-Time Edge-Aware Denoising in Fluoroscopic Devices. BioMed Eng OnLine (under revision for publication)*
- *Centracchio, J.; Sarno, A.; Esposito, D.; Andreozzi, E.; Pavone, L.; Di Gennaro, G.; Bartolo, M.; Esposito, V.; Morace, R.; Casciato, S.; Bifulco, P.: Efficient Automated Localization of ECoG Electrodes in CT Images Via Shape Analysis. IJCARS. (under revision for publication)*
- *Esposito, D.; Savino, S.; Andreozzi, E.; Cosenza, C.; Niola, V.; Bifulco,P.: The Federica hand. Res. Biomed. Eng. (under revision for publication).*

b. Conference papers

- *Andreozzi, E., Pirozzi, M. A., Fratini, A., Cesarelli, G., Cesarelli, M.; Bifulco, P. A Novel Image Quality Assessment Index for Edge-Aware Noise Reduction in Low-Dose Fluoroscopy: Preliminary Results. 2020 International Conference on e-Health and Bioengineering (EHB), IASI, 2020, pp. 1-5, https://doi.org/10.1109/EHB50910.2020.9280107*

- *Andreozzi, E.; Pirozzi, M. A.; Fratini, A.; Cesarelli, G.; Bifulco, P. Quantitative performance comparison of derivative operators for intervertebral kinematics analysis, 2020 IEEE International Symposium on Medical Measurements and Applications (MeMeA), Bari, Italy, 2020, pp. 1-6, https://doi.org/10.1109/MeMeA49120.2020.9137322*
- *Pirozzi, M.A.; Andreozzi, E.; Magliulo, M.; Gargiulo, P.; Cesarelli, M.; Alfano, B. 3D-printed anatomical phantoms for medical imaging applications: a methodological mini-review. Nordic Baltic Conference on Biomedical Engineering and Medical Physics (NBC 2020), Reykjavik, Iceland, 2020. (Article in press).*
- *Esposito, D.; Gargiulo, G. D.; Parajuli, N.; Cesarelli, G.; Andreozzi, E.; Bifulco, P.: Measurement of muscle contraction timing for prosthesis control: a comparison between electromyography and force-myography, 2020 IEEE International Symposium on Medical Measurements and Applications (MeMeA), Bari, Italy, 2020, pp. 1-6. https://doi.org/10.1109/MeMeA49120.2020.9137313*

5. Conferences and Seminars

a. Participation to the 8th International Conference on e-Health and Bioengineering, EHB 2020 (Iasi, Romania; 29-30 October 2020) and presentation of the paper "*Andreozzi, E., Pirozzi, M. A., Fratini, A., Cesarelli, G., Cesarelli, M.; Bifulco, P. A Novel Image Quality Assessment Index for Edge-Aware Noise Reduction in Low-Dose Fluoroscopy: Preliminary Results. 2020 International Conference on e-Health and Bioengineering (EHB), IASI, 2020, pp. 1-5, https://doi.org/10.1109/EHB50910.2020.9280107*

b. Participation to the 2020 International Symposium on Medical Measurements and Applications, MeMeA 2020 (Bari, Italy; 1-3 June 2020) and presentation of the paper "*Andreozzi, E.; Pirozzi, M. A.; Fratini, A.; Cesarelli, G.; Bifulco, P. Quantitative performance comparison of derivative operators for intervertebral kinematics analysis, 2020 IEEE International Symposium on Medical Measurements and Applications (MeMeA), Bari, Italy, 2020, pp. 1-6, https://doi.org/10.1109/MeMeA49120.2020.9137322*".

6. Activity abroad

I carried out a 6-month period of study and research (via smart working, due to the hindrances of the COVID-19 pandemic) under the tutoring of Dr. Antonio Fratini, senior lecturer at Aston University, Birmingham, UK. During my collaboration with Dr. Fratini's research group, I carried out part of my research activities on the improvements of noise suppression for low-dose X-ray imaging and on the Forcecardiography technique, which have been already described above.

7. Tutorship

a. Assistant for:

- B.Sc. course "Elaborazione di Segnali e Dati Biomedici" held by Prof. Francesco Amato (**20 hours**);
- M.Sc. course "Computer Interfaces for Biological Systems", held by Prof. Paolo Bifulco (**5 hours**);
- M.Sc. course "Strumentazione Biomedica", held by Prof. Paolo Bifulco (**10 hours**);
- M.Sc. course "Fondamenti di Ingegneria Clinica", held by Prof. Paolo Bifulco (**5 hours**).

b. Master of Science co-supervisor:

- I assisted Pasquale Lombardi (supervisor Prof. Paolo Bifulco), during the research activities for his Master Thesis in Biomedical Engineering entitled: “Metodi per la riduzione del rumore in immagini fluoroscopiche”.
- I assisted Vincenzo Punzo (supervisor Prof. Paolo Bifulco), during the research activities for his Master Thesis in Biomedical Engineering entitled: “Sviluppo e analisi di sensori di forza per il monitoraggio cardiorespiratorio”;
- I assisted Gaetano Chirico (supervisor Prof. Paolo Bifulco), for his Master Thesis in Biomedical Engineering on a wearable, wireless forcecardiographic sensor designed for cardiac monitoring (ongoing).