CALL:

SC1-BHC-06-2020:DIGITAL DIAGNOSTICS – DEVELOPING TOOL FOR SUPPORTING CLINICAL DECISION BY INTEGRATING VARIOUS DIAGNOSTIC DATA

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SUMMARY:

1 SPECIFIC ISSUE:

The interest and the knowledge of the medical field definitely have grown in recently among individual people. In addition to people who manifest a passion and a desire to become an active characters of this world, we have to add all those one who today, due to internet, think they can identify their diagnosis and then find or at least establish their own care looking for a confirmation by an interview with their doctor.

Once upon a time, the medical world was just for people who were the real actors of this world making medicine as their profession. So, the medicine world has changed profoundly by going from the doctor who healed and saved the ordinary people who relied on that as it is common doing with an institution, to the doctor who must treat them and who must confirm their supposed diagnoses generated by the navigation between sites distributors of notions as fast as unsure of modern medicine. At the same time a great change can be observed regarding the true medicine that one defined as science to deepen and to develop where the engineering or computer technology has brought, produces and will lead towards an improvement of the competences, of the knowledge and of the methods of intervention every time more effective and efficient. Within this latest concept it takes place the project that we want to start to help in developing a new approach to hospital diagnostic that assists healthcare professionals in their daily activities. The main argument of the project will be Additive Manufacturing and, more specifically, the 3D printing which are similar concepts in appearance, but different in reality. The final objective is the realization of a 3D printing technology center inside the hospital where will be introduced all machineries; In this centre, specialized staff will work in close cooperation with healthcare professionals, providing them with effective and efficient support with the objective, thanks to the hospital's presence of the specialized and advanced technology center, to raise the level of public health and then keep it continuously at the forefront.

The project is divided into distinct phases as individual activities, but united by the main vision of creating a hospital that can respond to modernity and new needs. Initially, it was observed the state of the current situation and, based on the photograph emerged, it was planned the work that will take place in order to achieve the objective. The first part of this phase will be entirely dedicated to the state-of-the-art analysis of scientific research in the field of the use of three-dimensional stamping technology (3D printing) in the medical subject and more in detail in the use of this technological tool as decision support for healthcare professionals in their diagnostic activity. Then it will be highlighted what could be the optimal use of the 3D printing tool in the hospital as a whole by mapping this situation for the individual clinics and divisions present. Therefore it will be necessary to underline the differences and the aspects that unite the different technical and technological needs of the individual specialist realities. In this phase will identify the main aspects on which working to integrate the current diagnostic methodology implementing technological support and various tools that will ensure at the end of the project the achievement of greater efficiency and effectiveness of such activity. This result will be useful to the doctor who can answer to the patient with greater knowledge of his clinical status due to have a more complete and detailed diagnostic response and then can take action faster and more precisely for the individual situation. Another aspect to study and analyze with great interest is the use of 3D printing technology in surgery always distinguishing the different clinical specializations and their singularities. In detail, we will highlight the effectiveness and efficiency in the use of this technology emphasizing how, being able to study more accurately and with more details the technical solutions to be used in different surgical procedures, there will be a decrease in the time required and a greater precision and accuracy in their execution. The last evaluation that will be faced in this phase will take care to find a place for the realization of the center of technological development of the sanitary unit and it will be analyzed all the logistic and safety aspects actions to allow this center technology to have all the necessary precautions and satisfying all human safety and legal regulations that must be respected. This involves an analysis and a search of sequence of plans of existing safety systems and that must be respected by positioning the structure of the technological center in one location or another within the health facility.

The same procedure will be carried out for the study of the legal aspect by choosing cutting-edge contractual systems that protect not only market innovation and competitiveness, but also the use and circulation of patients' personal data.

2. SCOPE:

a) IN THE MEDICAL FIELD

The second phase of the project is the direct consequence from the previous one indeed it will be compared all the results carried out from the analysis work and the study done and it will be start all the activities necessary to start the realization of the technological center.

From the study of scientific literature we will have been learned the different technological realities, most used and developed in the medical field, highlighting a range of possible tools, such as different equipment and different and innovative materials to produce prostheses, medical tutors, human organs and various equipment to speed up, improve and make more efficient the activity of the doctor and, therefore, also for patient's care. These results will be compared with the current methods of diagnosis in the hospital and compared with the needs of implementation to get the opportunity to ensure that doctors can deliver a much more detailed and accurate diagnosis to the patient. This result will bring benefits to the patient in terms of more detailed knowledge of his real health state and then a more specific and personal evaluation of the treatment to start. Also concerning to the medical treatment to choose it can be possible using a new technologies like producing personalized healthcare braces with materials that are more suitable and appropriated to the specific condition. This activity of comparison and synthesis will be conducted for all the individual clinics and divisions present in order to evaluate the possibility to implement an action aimed in supporting and improving the technological reality of the whole hospital, if possible, or even for making it more efficient in the technological and innovation aspects.

About the highlighted interest in using of 3D printing technology in surgical operations, it will be compared all those aspects of printing technology that will bring real and tangible benefits in this activity. Specifically, it will be strengthened the technology, up today used, obtaining as a first consequence the possibility of achieving a reduction in the time of intervention having available the organ to operate printed, better studying the real condition and then being able to plan with greater detail the type of intervention to be performed. In addition to the time it will be a cost reduction because it will be a reduction in the costs of anesthesia and staff that can be employed, in that time saved, for any other activity always necessary to the patient's health. Anyway, the greatest benefit is the possibility of using this technology: on one side we are able to print human organs, on which it is possible doing a more in-depth study, on other side we have possibility to print human organs to be transplanted during the surgery operation. This possibility help doctor to solve complex pathologies that once were impossible to treat and produce an increase in hope of healing to the patient. When the present technology to be implemented has been identified and the advanced and innovative one to be introduced within the hospital structure has been evaluated, it is possible to realize the technological centre within which this new technology and so all the individual machinery and all the different equipment and supporting structures, needed to carry out this new methodology of action previously described, will be positioned. First of all, an intranet VPN connection system (Virtual Private Network) will be created between the data collection centers of the individual machines, currently present on site, of the individual divisions and clinics in order to have a fast interaction between the different realities inside the hospital. Subsequently the technical and economic evaluation will be carried out and then the purchase of new machines providing an agreement of natural legal both for the installation phase and continuous or occasional presence of staff of external companies for maintenance or repair of the software and hardware of the above mentioned machines.

At the same time, research and evaluation will be conducted on possible technical candidates who will have to carry on this technological centre with dedication, precision and great commitment; therefore they must be technically capable persons, but also be able to show from the interview to have a enthusiasm or at least an interest in the subject, in order to ensure the presence within the laboratory of specialized staff, trained, but also stimulated in working with a certain fervor. Finally, some considerations should be given to the possibility of updating machines and staff to keep up with technology; in order to do this, it has been given the possibility of purchasing machines with long-term rental contract or with possibility to change the machinery in use with another one that has an updated software version, having already established some conditions for the withdrawal of the used.

b) IN THE LEGAL FIELD

From the legal side as well, this phase trickles down from the previous one and, necessarily, implies the choice of contractual systems suitable for the activities mentioned above.

The analysis of the international contractual landscape shows that Law no. 33 of 2009 governing the network contract, represents a unicum codified on the international scene.

Indeed, Article. 3 Paragraph 4 *ter* ss. L. n. 33/2009 establishes that: "*With the network contract, several entrepreneurs pursue the (common) purpose of increasing, individually and collectively, their innovative capacity and their market competitiveness and to this, on the basis of a common network program, they bind themselves to collaborate in predetermined forms and areas relating to their businesses, to exchange information or services of an industrial, commercial, technical or technological nature and to jointly exercise one or more activities falling within the scope of their business"*.

The *ratio* is, thus, that of formalizing, legally and economically, the spontaneous phenomenon of cooperation (based on ever-changing trust mechanisms that follow market dynamics): the market value that these entities have together is very different from the value of the individual bilateral contractual relationships. The network contract, in fact, was created with the aim of establishing more flexible relations between different legal entities, creating cooperation but, at the same time, maintaining competition (on this point it will be useful to analyze tax incentives and possible bank benefits).

In Italy, starting from the studies on the negotiation link, namely "Contractual network", different legal entities are aloud - leaving their legal independence unchanged - to set up bilateral contracts aimed at achieving a common goal: it will be useful to formulate a *business plan* from which strategic objectives, phases, profits and utilities will emerge and will derive to the network (associative contract with common purpose) and to the individual components that will be part of it.

The common program and the implementation regulations will have to deal with collaboration, multilaterality, openness, mutual or gainful purpose, multi-sectorality and the presence of moments of data exchange within the common program: with reference to this aspect, a technical screening on the correct use of personal data in the privacy field will be necessary.

3. EXPECTED IMPACT AND TYPE OF ACTION:

a) IN THE MEDICAL FIELD

The main result of this project is obviously the introduction into the medical world of the technology of ADITIVE MANUFACTURING or more specifically the use of the methodology of 3D printing that, as I pointed out before, are different.

The term ADDITIVE MANUFACTURING indicates a new production process that involves the aggregation of material for the realization of any object transforming what was the typical implementation procedure that provided for the subtraction of material. With the introduction of additive manufacturing methodology in addition to a new concept of production is also born a different design idea that focuses on the realization of the reticular structure and leather that surrounds this structure making the objects more light but at the same time able to resist the efforts . Then it starts a study of new materials to make products using this new technology; it is easier produce new materials because we can create special materials making a mixture or union of different percentages of each powdered elements with possibility to ensure to our products specific characteristics desired and previously studied. This led to a real conceptual revolution in manufacturing. The term 3D Printing in particular means the realization of three-dimensional objects through additive production, starting from a 3D digital model produced with CAD (Computer-Aided Drafting) /CAM (Computer-Aided Manufacturing) software dedicated and then elaborated arriving at the creation of the STL format (Standard Triangulation Language) to be realized through a 3D printer . It is then initially used to speed up the realization of prototypes (hence the concept of rapid prototyping). 3D printing is born in the 80's and more precisely with the publication of the patent of Chuck Hull that invents the SLA (Stereolithography). Subsequently there were further evoluptions and developments with the introduction of different techniques of stratification of the material and with the use of countless other materials with their own mechanical characteristics that allowed the spread of 3D printing in various sectors, different from each other, ranging from the mechanical field with the production of components in the automotive and aerospace fields, to the sports field with the realization of part of frames of bicycles, to the sanitary field up to the realization also of furnishing objects.

By deepening the concept of Additive Manufacturing, individual processes are identified that differ in their production method of the single layer and that differ depending on the material and technology of the machine used. Then, in 2010, the American Society for Testing and Materials (ASTM) group "ASTM F42 - Additive Manufacturing" created a set of standards that classify the range of additive manufacturing processes by dividing them into 7 categories (Standard terminology for additive manufacturing technologies, 2012) briefly described below.

VAT Photopolymerisation

To this category of additive manufacturing process belongs the technology called SLA (Stereolithography). By immersing particular photosensitive polymeric resins, able to solidify if selectively affected by a beam of point light coming from a source of UV (ultra violet) layer after layer, in a tank the bottom of which has the possibility to descend or rise by a single step once solidified the single layer. It does not need any supporting material. The produced objects are characterized by a high resolution and a very smooth surface. Very similar is the technology

DPL (Digital Light Processing) that differs from ALS only by using a projector instead of a single beam to hit the resin with light and activates polymerization throughout the layer instead of hitting point by point and to be more advantageous for components with large size and few form details.

Material Extrusion

Fuse Deposition Modelling (FDM) is based on material extrusion technology. The heated and malleable material in a semi-solid state is deposited through the nozzle of an extruder, layer by layer from bottom to top, on a platform that moves vertically along the z-axis. The nozzle, moving parallel to the platform, draws the object to be realized. In this technology for the realization of objects there is a need for the creation of support whose material is also deposited in the form of a semi-solid layer which then always solidifies through a nozzle. Compared to the excellent chemical and mechanical properties, because the filament layers are evident , the surface finish of the products made with this technology appears raw and to improve it it is advisable to apply a sandblasting or chemical abrasion. The main material used in this technology is acrylonitrile butadiene styrene (ABS), but polylactic acid (PLA) is also used in pure form or, due to its excellent adhesive properties, also in the form of composite

Material Jetting

Similar to 2D inkjet printer technology in this category is the Multi Jet Modelling (MJM) or Polyjet Modeling (PJM) technology with which liquid acrylic polymers are laminated on a construction platform with a print head with one or more nozzles and treated by exposure to UV lamps. The print head moves through the platform in predefined paths from a CAD model during the process until a layer is fully printed. Because the material must be deposited in drops, the number of materials available for use is limited. Only polymers and waxes with a particular viscous nature and droplet-forming capacity may be used. The parts realized are of high aesthetic level and, in the case of some specific photopolymers and resins, they also possess medium-high mechanical properties. Here, as in the case of FMD technology, a material is used to support the realization of the object, which must then be separated from the object itself.

Binder Jetting

The technology of this category consists in the spraying of binding materials: a liquid binder is applied with printing heads that strategically deposit droplets of binder in the powder bed of the base material with which to make the object. Layer by layer the printing head that moves on a horizontal plane compacts the single layer of dust and after the printing plate lowers is laid a further bed of dust of the material to be compacted. The process is repeated until the part is completed and the unused dust is recycled. The product obtained with this technology requires a subsequent post-processing, such as sintering and infiltration, to improve its mechanical characteristics. In addition to metals, the casting of the binder operates on a range of other materials, such as sand, ceramics or plastic.

Powder Bed Fusion

This category presents different production technologies. In general for the melting of the powders a laser or electronic beam is used; In detail we have the Selective Laser Sintering (SLS) where a fixed laser directs the beam to a moving mirror and hits the powder which is sintered by binding to the surrounding grains with molecular bonds. It can be used with different families of materials, such as polymers, composite materials, ceramics and some metal alloys. Direct Metal Laser Sintering (DMLS) and Selective Laser Melting (SLM) use a laser system that draws on the surface of an atomized metal powder, melting the part that later solidifies. After each layer, a blade adds a new layer of powder and repeats the process until the final metal parts are formed. The two technologies allow to realize prototypes directly in metal, ready to be tested; however, they need a finishing process in order to be used as finished products. The only difference is that SLM melts metallic powders into a homogeneous mass instead of sintering them. The only technology that uses the electronic beam is the Electron Beam Melting (EBM). The electrons are directed along the set trajectory by passing them between two rotating ring magnets and then hitting the dust bed. It can only be used with pure metallic powders without additive substances. The parts made by sintering (SLS and DMLS) compared to those made by melting (SLM and EBM) have a greater porosity and a less homogeneous molecular structure from which derive even worse mechanical characteristics.

Directed Energy Deposition

The principle underlying this category is the simultaneity with which the parties are created and deposited. This category includes Laser Engineered Net Shaping (LENS) and Electron Beam Additive Manufacturing (EBAM). The first uses a laser to melt the metal powder delivered simultaneously to the laser and from the same nozzle with the presence also of a pressurized inert gas to protect and control the properties of the melt and to promote the adhesion layer to layer providing a better wetting surface. The second one replaces the laser with an electron beam. The process can be used with polymers, ceramics, but is typically used with metals, in the form of powder or wire.

Sheet Lamination

The two technologies present are Ultrasonic Additive Manufacturing (UAM) and Laminated Object Manufacturing (LOM). The first uses metal sheets or strips, which are bonded together with ultrasonic welding and subsequently an additional CNC machining and non-alloy metal removal is required. The LOM uses a similar layer-by-layer approach, but uses paper as a material and adhesive instead of welding. The LOM process uses a cross-hatching method during the printing process to allow easy removal of non-alloy metal.

In this last phase of the project it will be performed the work of divulging the reality just realized and then it will be published the results of the benefits obtained from the use of the new technologies introduced in the daily hospital activity. On the one hand, it will be disseminated information on the technical aspects of interventions performed with the help of new methodologies, included within the hospital structure, highlighting the improvements made and the benefits produced by the possibility of dealing with interventions previously not achievable or that would have presented greater risks of no positive result. On the other hand, it will be shown the advantages that the technological evolution introduced in simple diagnostics will have on the reconstruction of more certain symptoms and on the choice of more targeted and personalized care. All this it will be argued and supported by the inclusion, in the evaluation of the results of the advantages obtained, management, time and economic aspects. It will show how this technological aid will produce, against an initial economic investment, a return on the general economy certainly profitable by reducing the time for execution of individual activities, by reducing the use of some of the materials previously most used and ultimately by achieving a more efficient and productive management of the economic and material resources of the entire healthcare unit.

b) IN THE LEGAL FIELD

In view of the expected impact, this project implies a careful examination in the field of personal data protection (UE Regulation 2016/ 679 c.d. GDPR).

Indeed, the exchange of data requires an in-depth study regarding the qualification of the subjects involved in the agreement, the territorial location of the owners (in European or non-European context), a legal basis in the processing of the data and technical and organizational security measures adequate to the risks.

As for the qualification of the subjects involved in the agreement, the relationship can be of three types: the presence of an owner and a manager, co-ownership and autonomous ownership.

The choice of the contract to be stipulated must necessarily consider the legal qualification of the subjects who will process the data. This project, therefore, will allow for the analysis of the owner role (determining means and ends of data processing) and that of the manager (the person who processes data on behalf of the owner), of the co-owner (in which the subjects together determine the purposes and means of the processing) and of the autonomous owner – preferred for the network contract – in which each owner determines the means and purposes of data processing in different ways.

The second aspect to consider will focus on the territorial location of the different owners (within or outside the European Union): in case the subjects and instruments used are all located within the EU, the applicable regulation will be the one common to the GDPR.

Otherwise, the instruments provided by the GDPR will be applied for the cases that provide the transfer of data to foreign countries such as, for example, the standard contractual clauses.

As for the legal basis to be applied, this will be the prerequisite on which the processing of personal data will be based: the legal basis mainly depends on the type of data to be protected, which in this case, concerns the particular data.

Furthermore, it must be asked whether the legal basis required by the scientific research framework may or may not be that of consent.

Ex art. 32 GDPR, risk analysis of the performance of the personal data processing activity will be carried out (in this case, particular medical data or biometric data): the owner and the manager of the data must adopt security measures appropriate to the risks for the interested parties.

Therefore, given the absence of a definition of risk in the European Regulation, the non-binding legislation ISO 31.000 from which to deduce a definition of risk can be consulted (that, at first glance, is a possible negative or positive effect of the process) and, then, organizational techniques appropriate to the risks suitable to protect the possible violation of the data subject's rights and freedoms must be adopted (the risk will be calculated by multiplying the impact probability and will be assessed on the basis of the four parameters of confidentiality, integrity, availability and resilience of the data).

Lastly, the study of the impact value (low, medium or high) of the particular data processed with reference to the nature of the data, the categories of data subjects and the purpose of the data will be of significant importance. If a high risk emerges from the analysis, an impact assessment will be necessary "Data Protection Impact Assessment", deeper and more extensive evaluation than the risk analysis.

Moreover, this phase will be useful for the study of the drafting of the contract and for the choice of its essential elements. The analysis of the contractual structure must indicate the strategic objectives, the method of measuring the work's progress, the common network program (through the collection of strategic objectives), the duration of the project and the possible subsequent adhesion of other participants interested in the project.

As to the form the contract must take, the possibility of simplifying the drafting mechanism of the articles of association will be examined by the technicians, allowing the use of a digital form (thus guaranteeing the simultaneous adhesion of physically distant subjects). Finally, a diligent study of the publication of the contract will be useful in order to ensure transparency and clarity for the community by means of public registers.

In addition to the essential elements, it will be useful to verify the inclusion of optional organizational elements on the basis of the equity content and the *governance* adopted.

Finally, it will be necessary to choose the consistency of the network from a qualitative and quantitative point of view and, therefore, to choose whether to apply a light, medium or heavy one.

The first type of network will guarantee a mere exchange of useful information since there is no common fund and the participants, consequently, will not be able to enjoy any tax relief, on the contrary the classic joint and several liability regime will apply *ex* art. 2047 c.c..

The medium network, on the other hand, will use the discipline of the consortium with external activities pertaining to art. 2641 c.c. with the possibility of using the limited liability regime to guarantee the solvency of the bonds by the sole means of the mutual fund, without affecting the assets of the individual legal entities.

Finally, the heavy network is characterized by the presence of the common fund and the common *governance* body to protect the economic and financial stability of the fund which, for these reasons, will provide the *network* with legal personality and its own assets.

The establishment of the common fund and the common body will be analyzed in detail to verify the need for the heavy network.