Medical Imaging Clinical Trials Unit: a professional need

Authors: Ana Penadés-Blasco[1], Sonia Ginés-Cárdenas[1], Amadeo Ten-Esteve[1], Pilar Bello Arques[2], Juan Mª Soriano Llobera[3], David Vivas Consuelo[4], Luis Martí-Bonmatí[1,2]

[1]Biomedical Imaging Research Group (GIBI230) and "La Fe" Imaging node of the Distributed Biomedical Imaging Network (ReDIB), Singular Scientific and Technical Infrastructures (ICTS), Valencia, Spain.

[2] Medical Imaging Department, La Fe University and Polytechnic Hospital, Valencia, Spain.

[3] Grup d'Investigació en Salut Pública-UPC (Polytechnic University of Catalonia).

[4] Research Centre for Economics Engineering, Universitat Politècnica de València, 46022 Valencia, Spain.

Address for correspondence:

Ana Penadés-Blasco,

La Fe Health Research Institute – La Fe University and Polytechnic Hospital,

Avda. Fernando Abril Martorell 106, 46026 Valencia (Spain).

E-mail: ana_penades@iislafe.es

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Abstract

Problem definition: The management of clinical trials requires special coordination and dedication among all actors involved. Lack of organisation can lead to situations in which the process can be seriously affected. To avoid these situations, it is crucial to have a properly designed management and control tool as well as a staff with well-defined tasks to efficiently manage the process of performing a clinical trial, which will result in a better quality of care for the patient.

Materials and Methods: A unit was created to efficiently organise the participation of our Medical Imaging Department in clinical trials. This entity was defined and monitored using a customized, flexible, modular software package that provides the information necessary to execute and monitor requests (appointments, protocols, reports, complaints, billing). Various indicators of activity and professional satisfaction were parameterised.

Results: From 2016 to 2020, 367 trials were participated and monitored, 50% of all the clinical trials at the hospital. The financial benefits of the Medical Imaging Department budget grew by 47% in this time. The coordination with other departments and principal investigators involved in the trials improved, as shown by surveys (62% fluid and 38% very fluid), and their perception of collaboration was 86%.

Managerial implication: The implementation and growth of a medical imaging clinical trials unit in a Medical Imaging Department involve identifying the tasks, personnel, organisational needs, workflow, monitoring and invoicing. The creation of this medical imaging clinical trial unit has improved the control and traceability of clinical trials within the Medical Imaging Department, as evident through indicators of higher success and fewer complaints.

Keywords: Management, Clinical Trials, Radiology, Nuclear Medicine, Efficiency, Clinical Imaging.

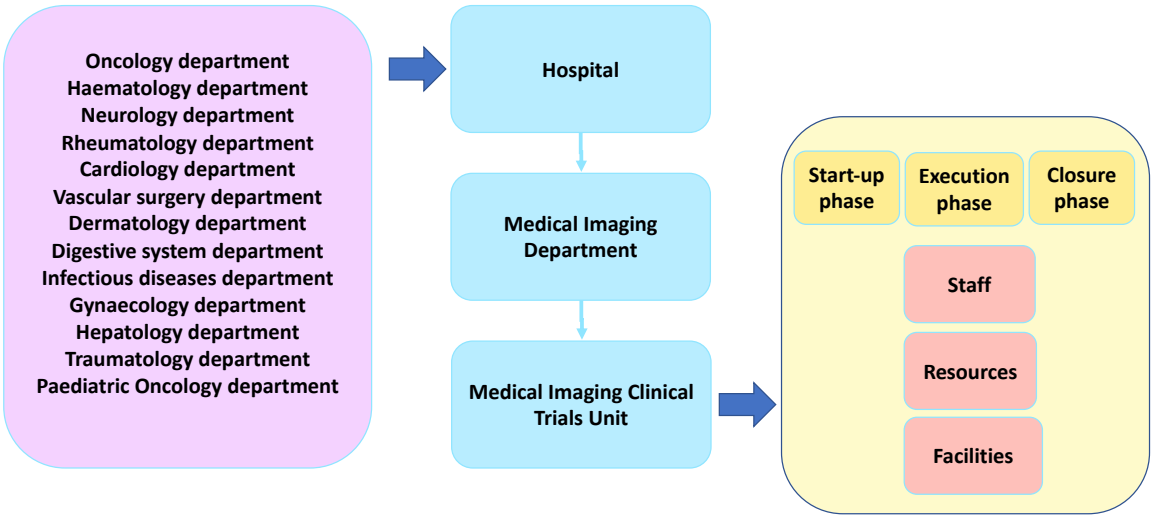
Introduction

Clinical imaging plays a fundamental role in many clinical trials, often involving specialists in both Radiology and Nuclear Medicine. Most clinical trials are randomised experimental studies that aim to evaluate the efficacy and safety of a treatment in a select group of patients (Clinical Trials 2019). In these populations, different imaging modalities are often used for the initial detection and staging of lesions, to assess the response to treatment, and to define adverse effects. In addition, imaging biomarkers are becoming more widespread and used to assess the biological effects of treatments with good statistical power (Wang 2005). All medical imaging modalities are now used in clinical trials, with Computed Tomography (CT), Magnetic Resonance (MR) and Positron Emission Tomography (PET) being the techniques most widely employed.

Most Radiology and Nuclear Medicine departments are involved by their clinical obligations to carry out the scheduled imaging studies but they are reluctant to add exams to the burden of their daily workflow. Nevertheless, radiologists placed much expectation on these units to actively participate in the clinical trials pathway and benefit.

Organisational strategies to establish clinical trials units that act independently on an operational and financial level have recently been adopted, with some even set up as companies external to hospitals and imaging departments. In our public university hospital environment, we created a Medical Imaging Clinical Trials Unit (MICTU) in 2016 within the realms of our Medical Imaging Department and following the structure shown in the Figure 1, with the aim of generating resources and of opening the possibility of contracting researchers through this unit. The MICTU was created to help structure and optimize the participation of the Medical Imaging Department in clinical trials that involve imaging procedures.

Figure 1. Structure and relationships of the Medical Imaging Clinical Trials Unit.



The MICTU was designed to perform the integrated management of clinical trials in which medical imaging is necessary to monitor the response to treatment. The unit is formed by a multidisciplinary team of 8 people contributing to a more efficient management of the clinical trials. In this paper, our objective was to describe how the MICTU was set-up, the resources it uses and its achievements over the past four years since its creation in 2016.

Materials and Methods

Here we will describe the tasks and organisational needs of the unit, the workflow, the staffing requests and the indicators of success that are considered relevant to assess the performance of the unit.

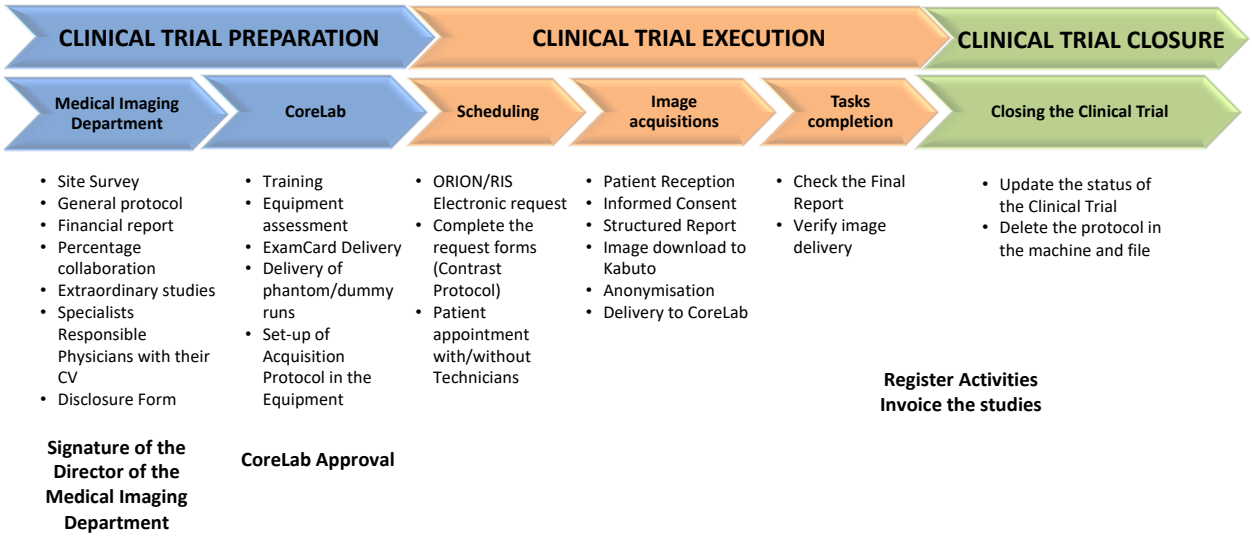
Tasks associated with the Medical Imaging Clinical Trials Unit

Clinical trials follow very meticulous protocols and thus, the main activities of the MICTU in relation to clinical trials were initially identified as:

- To store and share all the documentation necessary to perform the clinical trials.
- To handle all the imaging requests and to efficiently schedule image acquisition within the deadlines established by the protocol.
- To ensure and verify that the studies are performed with the adequate quality, and that the results are sent to the centralised imaging laboratory (CoreLab) within the required timeframe.
- To verify that the radiological reports comply with the specific criteria established in the clinical trials.
- To check that any corrections are adequately resolved within the deadlines established.

During the life cycle of clinical trials, the main tasks to be performed are identified, as well as the 3 main phases a clinical trial goes through: start-up, execution, and closure. The participation of the Medical Imaging Department in clinical trials should be structured based on the workflow outlined in Figure 2.

Figure 2. Workflow of a clinical trial in our environment with the main milestones



Start-up phase. Documentation required to commence the clinical trial

During this phase, the resources and the level of collaboration between the Unit, the principal investigator (PI) and the promotor of the clinical trial are established. The information and documentation related to the study should be compiled prior to commencing the clinical trial, ensuring it is available to Unit's staff. Among this documentation, the following should be essential:

- Site survey: information on the personnel involved in the trial, the role they play and the characteristics of the equipment used to acquire the images.
- Imaging protocol: guidelines for the correct performance of the imaging studies, including the main characteristics and technical specifications.
- Financial report: including the agreement between the promoter, the PI, and the beneficiary centre, stipulating the cost per patient and the indication of whether the studies are performed as ordinary studies or whether payment for extraordinary studies is contemplated. These extraordinary studies must be performed outside of normal clinical practice and their cost must be indicated in this report.
- Collaboration percentage: the financial agreement for the participation of the MICTU should be established, which does not usually exceed 15% of the cost per patient. This percentage is set out according to the workload and involvement of the Unit. In our case it was estimated to be waived if performed with normal procedures and standard clinical involvement; 5% if performed with normal procedures but there is any specific clinical involvement; 10% if performed with specific procedures but the standard clinical involvement of the healthcare professional; and 15% if both the procedures and the clinical involvement are specific to the clinical trial.
- Specialists in charge: this involves defining the physicians in the Medical Imaging Department who will be involved in the trial and responsible for reporting.
- Financial Disclosure Form: a form in which the associated medical staff must declare any conflicts of interest regarding their participation in the trial.

- Curriculum Vitae: a letter of presentation from the professionals participating in the trial that reflects their merits, studies, positions, work experience and research or other professional activities.

All this documentation must be validated by the Director of the Medical Imaging Department before the clinical trials can be carried out. This signature is essential for the Unit to participate in the clinical trial.

Start-up phase. Central Laboratory Approval

The CoreLab involved in the clinical trial must assess and validate the clinical imaging equipment to be used, the ability to identify and relabel the medical images and the quality of the images acquired (dummy or phantom run), considering the following issues:

- Training: explanation of the imaging procedures to the technical staff in charge of carrying out the clinical trial.
- Equipment assessment: assessment of the specific equipment to be used in the clinical trial.
- Acquisition protocol set-up: assessment of the acquisition protocol in the assigned equipment by sending the Protocol File (Examcard) to the promoter or CoreLab and through the acquisition of the phantom or dummy runs to validate the quality of the image.

The CoreLab must approve the centre prior to commencing recruitment and the analysis of the first patients in the clinical trial.

Scheduling

All imaging scans in a clinical trial are managed by the Unit to ensure that they are performed on each patient in a timely and appropriate manner (Chaithanya 2020). In this phase, the Unit must pay attention to the following issues:

- Receipt of the electronic request for an imaging study from the PI associated with the clinical trial.

- Completion of the information on the request form with the specific information related to the acquisition, report, and submission procedure, ensuring that all the relevant information is readily accessible to the MICTU staff involved in the study.
- Patient scheduling, ensuring that the scan is performed on the appropriate equipment and within the timeframe established in the clinical trial. Studies requiring the use of hospital-owned equipment are carried out in coordination with the hospital's appointment service. By contrast, data acquired on research equipment can be scheduled by the MICTU technicians' team. If feasible, patients will be scheduled in that equipment available only for research purposes (at our centre, a 3T MR and PET/MR).

Image Acquisition and Radiological Reporting

The Unit must ensure that the images are acquired according to the defined protocols (Farrell 2010) and that the specialist physician uses the appropriate response assessment criteria. The following aspects should also be evaluated:

- Physical presence of technical staff from MICTU to ensure proper positioning of the patient using specific templates for specific projections when necessary.
- Structured reporting in accordance with the specific guidelines to evaluate the response established in the clinical trial.
- The downloading, de-identifying and sending of acquired images to the CoreLab-enabled platform to be evaluated by an Independent Review Committee (Faunterloy 2001) or to obtain more complex quantitative metrics (Yankeelov 2016)

Completion of the tasks

This checkpoint serves to verify that all elements and tasks that are part of the clinical trial have been performed as agreed. Specifically, the Unit should:

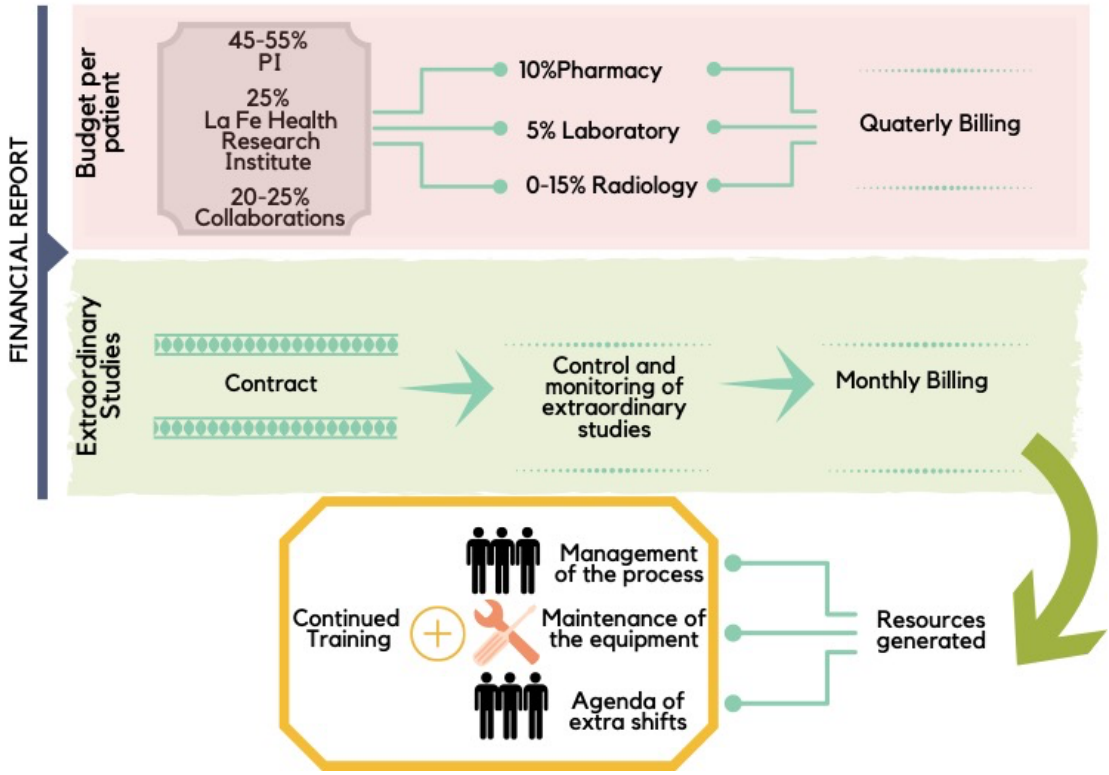
- Check that the images stored in the PACS were obtained following the acquisition protocol stipulated in the clinical trial, and that the reports were generated and stored in the hospital's information systems prior to the patient's medical visit to the PI's team.
- Check that the images were sent to the CoreLab.
- Check that the acquired images have been included in the Unit's activity register (generic annual Excel file of the imaging studies managed by MICTU).

Closing the clinical trial

When the clinical trial ends, all the information acquired must be collated to control and validate the quality of the activities carried out by MICTU. In particular, the following activities must be ratified:

- Update the status of the clinical trial in the Unit's control system with the labelling of "closed".
- Eliminate the specific acquisition protocols from the machine used and store them in an acquisition protocol repository.
- Collect the total activity generated (Excel format) corresponding to all the studies performed.
- Audit the studies performed by sending the activity recorded for verification by the promotor. At this stage it is important to recognise any additional imaging studies so that they are invoiced in accordance with the economic guidelines and following our financial management workflow shown in figure 3. Once the information has been collated, invoicing cane be carried out through the Institution's Invoicing Department, with payment tracking (iFundanet, institutional management tool).

Figure 3: MICTU financial management workflow



Workflow control

In order to carry out the tasks described in an efficient and structured manner, the web based Redmine software has been customised (Redmine 2021). This tool was initially designed for project management, but its customisation makes it possible to centralise all the information related to the documentation, procurement requests and programming of each clinical trial in a single data environment. In this way, it can be organised so that is easily accessible to all staff, and so that it permits the tracking of all the requests. The tool is particularly useful to obtain activity reports, activity statistics and to resolve queries given this capacity to track all the requests (Ten-Esteve 2017, Pinar Keskinocak 2019).

Redmine has become the management tool for MICTU and it is used for all the clinical trials in which MICTU participates. The main activities related to this tool are:

- To assign different user profiles: appointment requests only to PI team staff; access to procedures for the investigator's team; and full access to all study data reserved for the clinical trial management staff in the Unit.
- To review the most relevant information of the clinical trial: sponsors, EUDRACT, staff assigned to the clinical trials, contrast agents or radiotracers employed, acquisition protocols, image submission platform, etc.
- To check the status of the citations for each clinical trial
- To verify the uploading of the images generated to the corresponding platform.
- To supervise that no queries are generated and if so, the status of the query and the time it takes to resolve it.
- To compile a report of the activity carried out in each period.

Staffing needs

From its beginnings, it has been necessary to provide the MCITU with increasing professional resources. At present, multidisciplinary profiles have been defined as necessary to contribute to the specialist tasks defined, including Nursing, Technicians, Graduates in Business Administration and Management, and in Biomedical Engineering.

The Unit's Nursing post is responsible for carrying out the tasks included in the preparation and documentation phase of the clinical trial, guaranteeing the correct collection and availability of the documentation. In addition, it must perform tasks such as the administration of intravenous contrasts and any patient care necessary. The tasks assigned to the Technicians staff are related to the citation of the patients in the required time window, image acquisition following the specified protocol and the reporting in accordance with the specific criteria indicated. The Business Administration and Management staff monitor the operation and needs of the Unit, controlling the technical and human resources necessary for its proper functioning, and overseeing the monthly activities carried out and invoicing. The Biomedical Engineer is responsible for adapting the technical resources available to the

needs of the Unit, resolving technical incidents and adjusting the apparatus to the most complex acquisition protocols when necessary.

Key indicators of success

A battery of indicators selected to provide accurate and relevant information to assist in decision-making was constructed. These indicators were agreed on by the management team and they must be perfectly understandable by the entire team involved in their development, updating and use. In the Unit, indicators were generated for each of the clinical trial phases identified.

Clinical trial preparation phase:

- Average time to open a Clinical trial: this corresponds to the average time taken by the Unit to generate the necessary documentation and carry out the necessary procedures to set up a Clinical trial so that patients can be included in the study. This information can be obtained by recording the number of days elapsed between the incorporation of the clinical trial, the provision of the necessary information and setting up the equipment required to carry out the studies.
- Number of clinical trials opened annually: this number corresponds to the clinical trials in which the MICTU collaborates each year. This data is obtained from the registration of the studies in the Redmine management tool.
- Queries generated in this phase and response time: the corrections in this preparative phase are generally due to the lack of document(s) necessary to start the study or the need for specialised technical assistance given the complex acquisition protocols that must be introduced into the equipment. To extract this information, the queries register created for this purpose in Redmine is used.

Clinical trial execution

- Total number of imaging acquisitions per year: this indicator covers the total number of acquisitions handled by MICTU that are reflected by the requests generated within Redmine.
- Number of acquisitions per imaging modality per year: as in the previous indicator, this index is extracted from the requests channelled and subsequently exploited through Redmine.
- Average citation allocation time: this corresponds to the time elapsed from when the PI's department requests the acquisition (status of the request as "new"), the specific day assigned by the Unit and the time to generate the request (status of the request as "quoted").
- Queries generated in this phase and the response time: the corrections in this phase are mainly due to errors in patient appointment requests. These may arise for multiple reasons, such as errors in the time point at which the patient is included in the request, errors in the selection of the modality by the PI's department, errors in carrying out the study (e.g., not following the acquisition protocol).

Finalization of the clinical trial

- The number of extraordinary acquisitions generated per year: these are requests for acquisitions channelled through MICTU that do not fall within normal clinical practice and therefore, they should be considered as extraordinary. These acquisitions and their associated costs are included in the financial report signed by the Institution and the Pharmaceutical Company responsible for the clinical trial, and to which the Unit has access. These activities and their associated costs are included in the database for subsequent invoicing.
- Annual amount generated (related to the activities of the MICTU and La Fe Health Research Institute): this indicator is related to the previous one and to the total amount generated by the management of the trial. This indicator includes a breakdown between the amount generated with the equipment owned by the hospital and the equipment owned by our research institute.

- Survey to control the satisfaction with the specialist doctors and the PI's department (number of queries received): this indicator measures the quality of the service provided by the Unit, both that of the imaging studies requested, and that of the radiologists and nuclear medicine specialists in the Medical Imaging department. These measurements are obtained through a survey of satisfaction distributed to those involved.

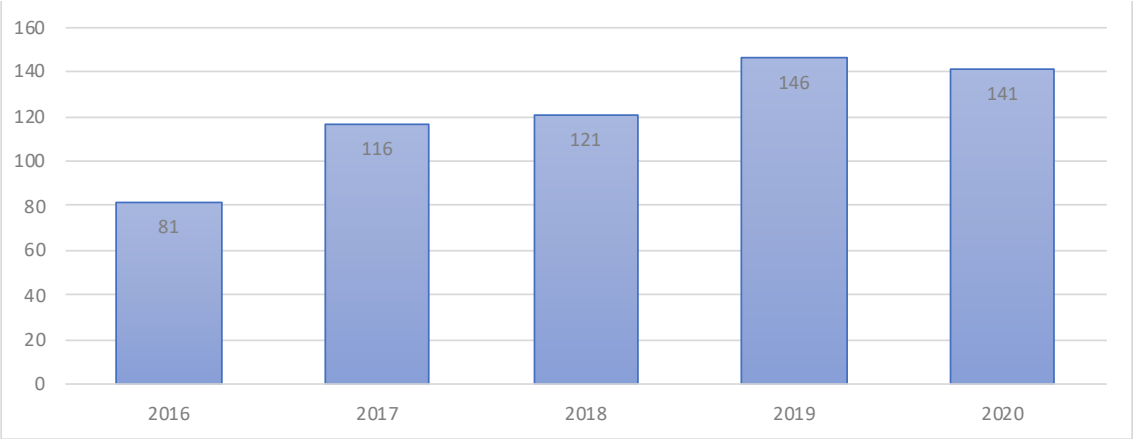
Establishing indicators to monitor the management work of the unit is fundamental as they help in decision-making and provide an overview of a complex structure. The indicators related to the acquisitions carried out reflect the evolution of MICTU activity, and they also enable decisions to be made when allocating the resources available and to assess the need to include new resources. With these units of measurement, an objective view of MICTU workload can be obtained that allows decisions to be taken when it comes to adapting resources.

The economic indicators enable the unit to visualise its overall status in terms of allocating and sustaining materials and human resources. The internal and external satisfaction indicators measure the quality of the service provided by the Unit, providing an overview of how the Unit is perceived both internally and externally. These satisfaction surveys provide the opportunity to highlight the weaker aspects of our unit and to receive suggestions for improvement that will help optimise the functioning of our unit.

In the preparation phase, we found that:

- The average time to open a clinical trial in our unit was 15 days from the request for collaboration to the Director of the MICTU signing the agreement.
- The number of clinical trials opened by our unit has increased from 80 studies in 2016 to more than 140 in 2020. The use of imaging studies in clinical trials has increased greatly, as seen in figure 4.

Figure 4: Number of clinical trials involving the use of imaging carried out



Regarding the queries received in this start-up phase, they were mainly for the following reasons:

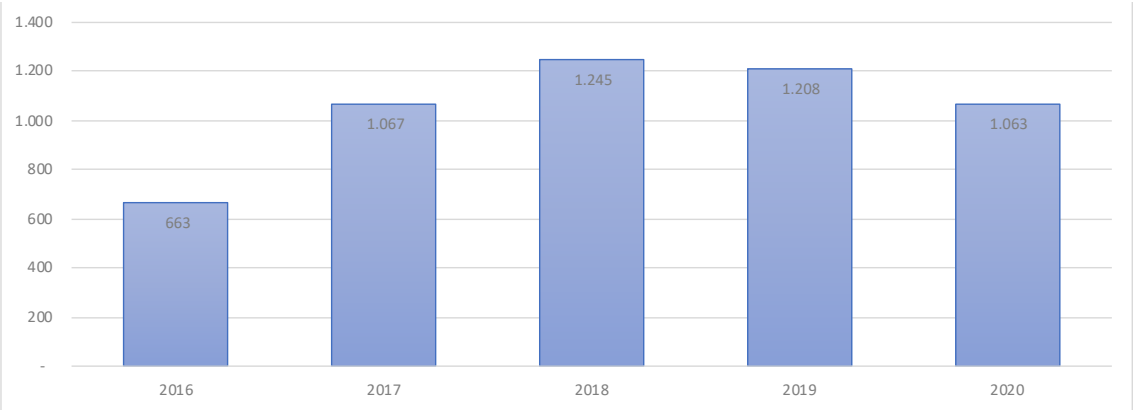
- 30% were due to a lack of the necessary documentation to open the clinical trial.
- 10% were due to the failure of some of the participants to sign the documents required to start the trial.
- 20% were due to other causes, such as discrepancies in the general protocol or acquisition protocol, or a lack of specificity in the protocol associated with the imaging techniques or the intravenous contrasts to be used.
- 10% were due to the late receipt of training certificates from staff assigned.
- 10% were due to the introduction of acquisition protocols with variants not previously established in the protocol.
- 10% due to errors in the procurement of phantom runs and a further 10% due to errors in the first acquisition of the volunteer or dummy run.

The average resolution time was 4-5 days depending on the initial investigator assigned and the ease of contact.

In the execution phase of the clinical trials, due to the COVID-19 pandemic the activity of our Unit decreased in 2020 relative to 2019 by 145 acquisitions, almost a 12% decrease in our activity.

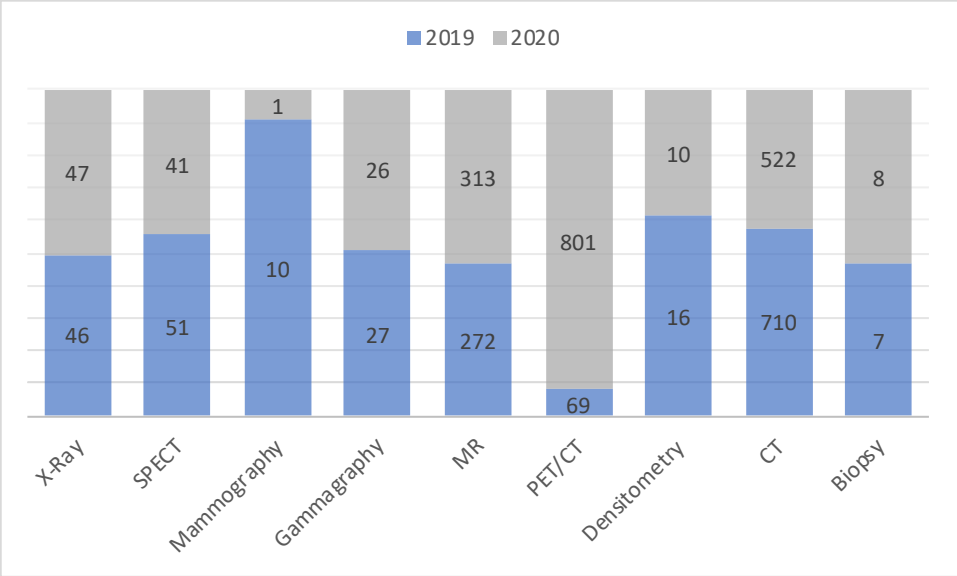
Therefore, while our activity increased steadily between 2016 and 2018, it stagnated and decreased from 2019 onwards, coinciding with the state of emergency due to the COVID-19 pandemic (see figure 5).

Figure 5: Number of imaging studies from all modalities handled by year.



In terms of the total number of acquisitions in each modality, we can see that CT was the main modality used in our Unit up to 2019, although we saw a change in 2020 when PET/CT becoming the most used acquisition mode (see figure 6).

Figure 6. Activity per modality



Regarding the average allocation time for patients included in a clinical trial, the time differed depending on the imaging modality to be performed, with Nuclear Medicine modalities those requiring most time. The average value was approximately 3 days from the time a request is received by our Unit.

Of the queries in the execution phase, 30% referred to citation, mainly due to errors in the citation request. These errors were mostly due to errors in the timing of acquisition, patients who underwent acquisition without going through the trial and following usual clinical practice, and who are then later requested with a retroactive date or simply because the appointment could not be made within the established timeframe due to an excessive workload.

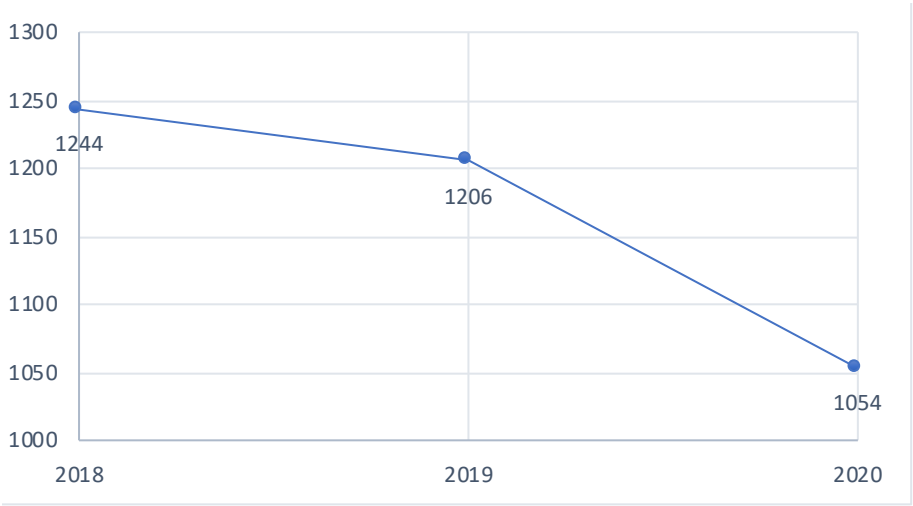
Errors in performing the imaging studies or in acquisition represented 40% of the total number of queries received in this phase. In these cases, we can differentiate between errors due to deviations from the acquisition protocol, errors due to patient movement, errors in the timing of the delivery of the contrasts or radiotracers used, or errors due to discrepancies between the Data Transmittal Form (DTF) and the image, all of which are considered as acquisition errors.

Errors in de-identifying and in the transmission of the imaging studies account for 15% of the queries in this phase, and they are mostly due to errors in the platform, errors due to incomplete de-identification of the patient's data, and errors in the internal identifiers (IDs) of the images in the trial. In summary, in this execution phase, 30% of the queries are associated with citations, 40% with acquisition, 15% with de-identification/submission and 15% due to reporting.

The average response time in this phase was 3 days.

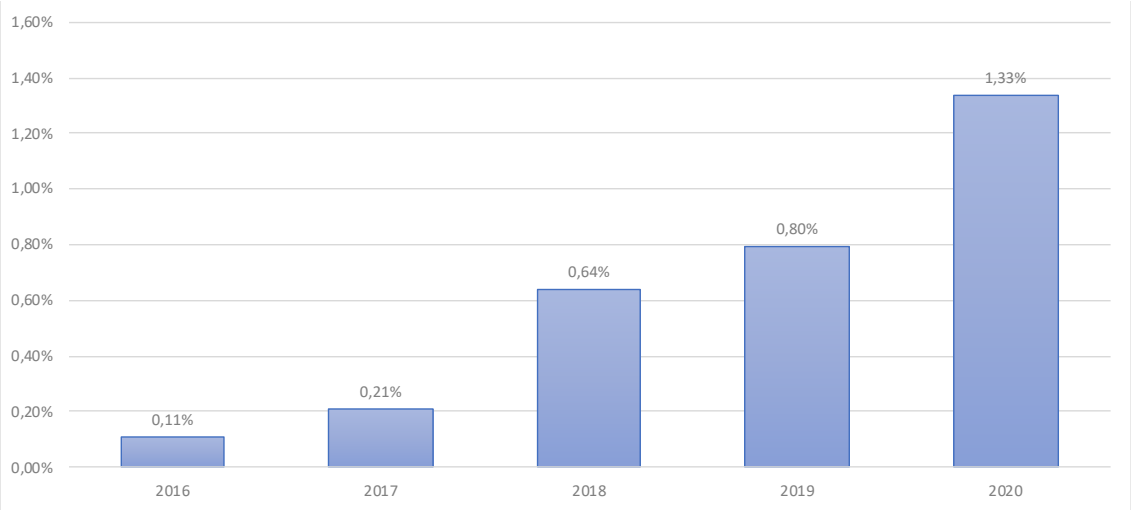
In the closure phase we distinguished a series of indicators that are extremely relevant to detect trends and decisions in the reallocation of resources. These indicators included extraordinary acquisitions handled by MICTU, which exclusively measures the imaging studies considered to be extraordinary based on the economic reports provided by the clinical trial promoter (see figure 7).

Figure 7.- Extraordinary studies handled by the unit each year



In reference to the resources used in the closing phase, a comparison was made between the overall annual budget managed by the MICTU and the economic resources generated by the Unit. The aim of this comparison was to define the resources that the Units dedicates relative to its overall budget and to monitor its evolution (see figure 8).

Figure 8. The income generated by the MICTU relative to the budget assigned to the Medical Imaging Department.



As can be seen, MICTU has experienced a constant growth since 2016 and its weight with respect to the budget managed by MICTU stands at 1.33%. It should be noted that the resources obtained through this Unit are mainly dedicated to the ongoing training of the healthcare professionals involved and to guaranteeing the sustainability of the Unit's resources.

The quality of the clinical trial management process in our unit is very important as it directly impacts on the quality of care for our patients (Chandrasekaran 2012). The quality of the clinical trials registered in our Unit is measured through the surveys of satisfaction carried out in the different departments of the Hospital.

These surveys address issues such as:

- Communication and collaboration between the MICTU and the PI's department.
- Ease of use of the Redmine tool to request and monitor appointments.
- Response times and agility in dealing with study requests.
- Delivery of study results on time and in accordance with the criteria established in the clinical trial.

- Aspects for improvement within the MCITU

These variables were analysed through a survey launched to a sample of 58 users, of which only 36% responded. In terms of the accessibility of the Unit, 62% of the results obtained were categorised as easy to contact and 38% stated full accessibility of this unit when required. No response was recorded related to problems with contact: “sometimes it is complicated or impossible task to contact the Unit”.

Regarding aspects such as the willingness of the MICTU to support the resolution of possible incidents, 86% of the responses indicated that the Unit was a collaborative service insofar as the resolution was a consequence of its management. Only 14% of the respondents indicated that the unit was sometimes uncooperative, and it was not always available to resolve problems.

Regarding the second point of the survey, more than half of the respondents (67%) considered the use of the Redmine tool to be useful or very useful in terms of the requests and the follow-up of patient appointments, indicating it was an easy tool to use.

Regarding the appointment response times, 57% of respondents rated the appointment time as adequate or very adequate, with 52% of respondents recognizing that the imaging modality influences the delay in appointment allocation. The imaging modalities that caused most problems in appointment allocation were PET-TAU, PET-Amyloid, FEVI and CT. The response time of the MICTU following consultation by the PI’s department was rated as good or very good by 62% of the users, while 24% described it as average. It should be noted that in response to the question “Have you received an explanation for the delay in response?”, 90% stated that the MICTU always offered information regarding the incident.

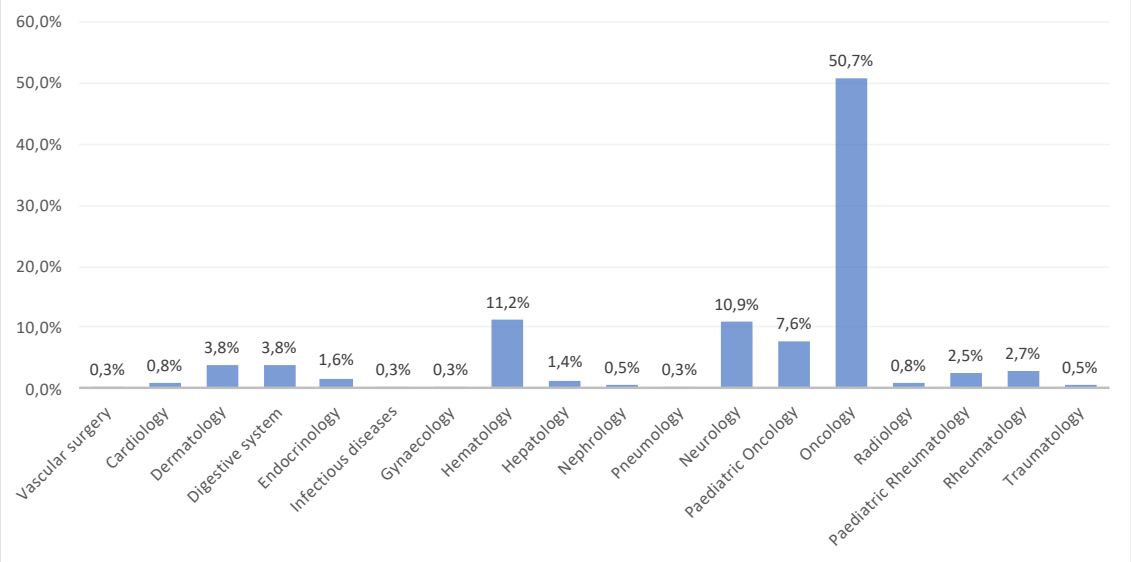
Nearly 62% of the responders stated that the acquisitions were carried out without incident and following the established protocols, while 38% stated that at some point there had been some kind of incident related to the acquisitions they coordinated and/or managed. When evaluating the de-identification and image sending times, the Unit was rated with a 76% level of satisfaction, classifying the times as adequate.

Finally, in terms of improving the MICTU to provide a better service, the survey highlighted some specific issues:

- Priority should be given to scheduling for screening tests and for the reporting the results.
- RECIST evaluations might generate problems, as lesions changed at the evaluations and target lesions might not be correctly registered.
- Periodic meetings are proposed to co-ordinate the ongoing trials and the procedures involving different parties.
- Implement MR with sedation, as patients with certain pathologies deteriorate and benefit from this treatment.

The main clinical trials handled by our unit and surveyed here were related to Oncology (50.7%), Haematology (11.2%), Neurology (10.9%), Paediatric Oncology (7.6%), Dermatology and Digestive pathologies (3.8% each) (see figure 9).

Figure 9.- Main departments requesting studies, shown as the percentage of clinical trials by departments in 2020



The main results obtained in the Unit over the continuous improvements are as follows:

- The workflow has been significantly simplified thanks to improvements in its design and its adaptation to the management tools used.
- The errors made in the Unit have decreased significantly.
- The staff in charge of the clinical trials have become more specialised in well-defined tasks.
- The use of Redmine has enhanced the control of the activities carried out. In addition, it has allowed all the actions undertaken during a clinical trial to be tracked.
- The design and implementation of a battery of indicators for each of the phases through which a clinical trial passes provides an accurate global vision of the situation in each of these phases, aiding decision-making.
- The implementation of quality control systems based on surveys of satisfaction has led to better communication between radiologists and clinicians. This translates into a better response for the patients included in the clinical trials.

Discussion

In recent years, targeted Clinical Trial units have been set-up at many centres, although there focus, and organization differs considerably. The IDIVAL Health Research Institute in Spain is a centre that do not have specific imaging equipment dedicated to clinical trials. For the execution of the clinical trials, IDIVAL team consists of 8 staff members who collaborate with the hospital, this unit being integrated into the hospital's own care circuits (IDIVAL 2021). At IDIPAZ, the Research Institute of another Spanish university center, there is no clinical trials unit that focuses on imaging, but they provide services that supports the researchers in designing, setting-up, management, analysis and prepare financial reports (IDIPAZ 2021). These organizations represent the most frequent case, being composed by trials managers who specialize in and monitor clinical trials, supporting all the research groups belonging to the institution. Several other Clinical Trials Units are organised in a similar way, without having a specific unit dedicated to the management of imaging in trials. In another situation, VHIO incorporates

experts from the Medical Oncology Department, including radiologists, conducting clinical trials at a different university hospital (VHIO 2021), although no specific imaging unit exists. The staff includes study coordinators, data managers, sample managers, administrative and quality control staff and the distribution is based on the phase of the trials, as well as on the organs and oncological pathologies involved.

Of relevance, some of these units, including our, are members of the European Clinical Research Infrastructures Network (ECRIN), a public non-profit organisation that connects scientific partners and networks across Europe to facilitate multinational clinical research. ECRIN represents a link between clinical trial sponsors and researchers, as well as providing advisory and management services to overcome the bureaucratic hurdles of multinational trials, thereby improving the collaborations between the different actors involved.

If we analyze other clinical trial units in Europe and the rest of the world, we find practically the same composition and professional profiles. As references, we would like to highlight three centers standing out from the rest.

The Center for Medical Imaging (CMI) from the University College London Hospitals comprises nearly 30 research staff, compounding clinical radiologists, non-clinical basic scientists, and support staff (research nurse, radiographers, and administration). This center has also a technical facility with a 3T MR and PET/RM systems (CMI 2021). This center stands out as an exclusive medical imaging center and has high-performance imaging equipment for use in clinical trials, as does our center.

The National Cancer Imaging Translational Accelerator (NCITA) is a UK national network of clinical research imaging infrastructures supported by a Cancer Research UK Accelerator Award. One of its cross-institutional units is related with the Imaging Clinical Trials Unit, which supports and coordinates studies where imaging is required. In addition, this Unit works closely with the Quality/Control Unit and the Repository Unit. The structure of this Unit is composed by a Director, a General Manager, a Statistical collaborator, and clinical trial practitioners (NCITA 2021).

The Clinical Trials Unit (CTU) is a central facility of the University of Freiburg's Faculty of Medicine and Medical Center. The unit is integrated into the clinical departments at the University Medical Center through fixed structures and has a distribution where a working Group in Clinical Trials coexist with the Head of the Unit. The Project Management Clinical Trials reports directly to this position and consist of a Project Management area, Project Assistance, Clinical Monitoring and Study Nurse Services (CTU 2021).

For any targeted imaging clinical trial unit to function properly, it is essential to establish a collaborative environment that involves the hospital's management and the main healthcare departments involved in the clinical trials. In addition, this unit must be equipped with the necessary human resources and management tools. In our experience, Redmine has been pivotal in controlling and monitoring the clinical trial activity at our centre, as well as allowing very efficient communication with clinicians and clinical trial managers. It is also significant that this system enables financial control of the economic resources to be distributed in a transparent environment. In this regard, automating the process of extracting costs for extraordinary tests has not yet been addressed in our MICTU, which would ultimately help further simplify and control this process. In addition, it is essential to reinvest the resources obtained in MICTU in those activities and professionals that offer added value, including access to training and strategic resources deemed necessary for all the staff involved in the trials. In our experience, the satisfaction perceived in the involved departments, and the visibility and capabilities of our Medical Imaging Department, have improved notably thanks to the involvement of all its members in the tasks assigned, as well as the specialisation of the staff.

The technological revolution in the medical field that has taken place in the last decade has attributed an important role to imaging in clinical trials. Indeed, it is recognized that medical imaging has an important and growing role in the development of new drugs (Thomas 2016), and that it is increasingly useful in clinical trials (Hernan 2008). According, the use of imaging to non-invasively assess the response to new drugs and devices is becoming increasingly important. The importance of medical imaging in clinical trials is reinforced by its reliability in evaluating the changes induced by

interventions through radiological measurement and the implementation of Recist 1.1 criteria, enabling disease evolution and drug effectiveness to be specifically evaluated (Tofts 2011, Neri 2016, Hernán 2016). Radiomics also helps in this assessment as it is the science that studies tissues, organs and lesions from their images, defining relevant phenomena that can be extracted from images through which predictive models can be constructed based on anatomopathological correlations (Grimaud 1996). In view of the possibility of developing more objective and quantitative parameters in the images obtained, there are many advantages to performing these tests in clinical trials. Therefore, on the basis that the increased activity in recent years is likely to continue, imaging clinical trials must be created and foster to implement this technology, collaborating as trial organisers and acting as centralised core imaging laboratories open to the national clinical trial network (Velibor 2019).

In conclusion, the creation of a Medical Imaging Clinical Trials Unit focused on the integral management of images represents added value in the clinical trial execution chain. These units should be member of national and international collaborative networks, offering new opportunities to reinforce the role of imaging in trials by establish new relationships.

References

Aravind Chandrasekaran, Claire Senot, Kenneth K. Boyer. (2012). Process Management Impact on Clinical and Experiential Quality: Managing Tensions Between Safe and Patient-Centered Healthcare. Manufacturing & Service Operations Management 14 (4) 548 566

Chaithanya Bandi, Diwakar Gupta. (2020). Operating Room Staffing and Scheduling. Manufacturing & Service Operations Management 22 (5) 958-974

CMI. Centre for Medical Imaging explanation. Accessed July 2021 https://www.ucl.ac.uk/medical-imaging/

Clinical Trials (2019) Learn about clinical studies. Accessed July, 2021.https://www.clinicaltrials.gov/ct2/about-studies/learn

CTU. Clinical Trials Unit of the Medical Center. Accessed July 2021. https://www.uniklinik-freiburg.de/zks-en.html

Farrell, B., Kenyon, S. & Shakur, H. (2010) Managing clinical trials. *Trials* 11, 78

Faunterloy, M. (2001), Submission of images to the centre for biologics evaluation and research in support of license applications for therapeutic agents. *Journal of clinical pharmacology*, 41.S7: 119S-121S

Grimaud J, Lai M, Thorpe J, Adeleine P, Wang L, Barker GJ, et al. (1996). Quantification of MRI injury burden in multiple sclerosis: A comparison of three computer-assisted techniques. *Magn Reson Imaging*. 14:495–505.

Hernan A, Walter C, Willett A, Manson A, Robinsa H, (2008). Observational Studies Analyzed Like Randomized Experiments. An application to postmenopausal hormone therapy and coronary heart disease. *Epidemiol*. 28:19-60

Hernán MA, Robins JM. (2016). Using Big Data to emulate a target trial when a randomized trial is not available. *Am J Epidemiol*. 183(8):758-64.

IDIPAZ. Platform's information: Research and Clinical Trials Unit. Accessed July 2021. https://idipaz.es/PaginaDinamica.aspx?IdPag=187&Lang=EN

IDIVAL. Clinical Trials Unit information. Accessed July 2021. https://www.idival.org/en/Soporte/Ensayos-Clínicos/Unidad

NCITA. National Cancer Imaging Translational Accelerator infrastructures. Accessed July 2021. https://ncita.org.uk/ncita-units

Neri E, Regge D. (2016). Imaging biobanks in Oncology: European perspective. *Future Onc*. 13:10-22.

Pinar Keskinocak, Nicos Savva. (2019). A Review of the Healthcare-Management (Modelling) *Manufacturing & Service Operations Management* 22 (1) 59-72

Redmine (2021) General information. Accessed July 2021. https://www.redmine.org/

Ten-Esteve A, Alberich-Bayarri A, Ruiz-Martínez E, Martí-Bonmatí L. (2017). Integration a tool for manage of clinical trials in medical imaging departments. Presentation. March 2017 *European Congress of Radiology*

Thomas E, David A, Lawrence H, Schwartz S, Lieberman M, Buatti JM, et al. (2016). Quantitative imaging in cancer clinical trials. *Clin Cancer Res*, 22:284-90

Tofts P, Collins B, (2011) Multicentre imaging measurements for Oncology and in the brain. *H.J Radiol*. 84:213-26.

Velibor V. Mišić, Georgia Perakis (2019) Data Analytics in Operations Management: A Review. *Manufacturing & Service Operations Management* 22 (1) 158-169

VHIO. Clinical Trials at VHIO. Accessed July, 2021. https://www.vhio.net/clinical-trials/clinical-trials-at-vhio/

Wang, Y.-XJ. (2005) Medical imaging in pharmaceutical clinical trials: what radiologists should know. *Clinical radiology,* 60.10: 1051-1057.

Yankeelov, Thomas E., et al. (2016) Quantitative imaging in cancer clinical trials. *Clinical Cancer Research*, 22.2: 284-290.

Figure Legends

Figure 1. Structure of the Medical Imaging Department and Medical Imaging Clinical Trials Unit.

Figure 2. Workflow of a clinical trial in our environment and the main milestones.

Figure 3. Medical Imaging Clinical Trials Unit financial management workflow.

Figure 4. Number of clinical trials involving the use of imaging carried out.

Figure 5. Number of imaging studies handled.

Figure 6. Activity by modality.

Figure 7. Extraordinary studies handled by the unit each year.

Figure 8. The income generated by the Medical Imaging Clinical Trials Unit relative to the budget assigned to the Medical Imaging Department in 2015.

Figure 9. Main services requesting studies.