PICCOLO

Multimodal highly-sensitive PhotonICs endoscope for improved in-vivo COLOn Cancer diagnosis and clinical decision support

Deliverable title	Deliverable ID: D9.4
Public Final Report: Final progress report (technical and financial)	Due date: 30-09-2020
	Submission date: 30-11-2020
	Editor/Lead beneficiary (name/partner): TECNALIA
	Internally reviewed by (name/partner): TECNALIA

Abstract:

This final public report presents a summary of the activities performed in the period M19-M45 and an overview of the efforts and costs employed in the whole project.

Dissemination level		
PU	Public	X
CO	Confidential, only for members of the consortium and the Commission Services	

This project has received funding from the *European Union's Horizon 2020 research and innovation programme* under grant agreement No 732111

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1. Summary

1.1 Context and overall objectives of the project

Colorectal cancer ranks as one of the predominant cancers, affecting approximately 1:10 people during their life and causing almost 880,792 annual deaths globally in 2018. Specifically, adenocarcinoma represents more than 95% of all these cases. It is estimated that 20-40% of patients undergoing colonoscopy present polyps. Of these detected polyps 29-42% are hyperplastic, whereas the rest are neoplastic. Clinicians demand new diagnostic technologies to assist detection and discrimination of hyperplastic and neoplastic polyps and reduce recurrence rates.

The main objective of the project is the development of a fully-functional wide-field fluorescence based, OCT and MPT photonics endoscope for improving colorectal cancer diagnosis providing in-vivo image-guided biopsy capabilities and higher sensitivity and specificity than current diagnostic methods.

The development of this fully functional photonics-based endoscope will:

- Obtain unprecedented sensitivity and specificity (>99%, >95%) on the optical analysis of neoplastic colorectal lesions.
- Reduce by 40% the needs of biopsying of the polyps detected on a colonoscopy.
- Reduce the number of missed polyps by 30% including the most challenging flat lesions.
- Reduce re-interventions by 90% by assessing lesion infiltration and resection assessment in situ.
- Reduce the intervention costs by 30% per patient outcome.
- Facilitate and augment the presence of EU Photonics SMEs and companies into the demanding biomedical diagnosis market via the exploitation of the PICCOLO endoscope and its components.

PICCOLO consortium has worked through all the project pursuing these objectives. On the hardware side, enhanced wide-field imaging and probe integrating OCT and MPT technologies have been delivered. On the software side, a computer aided diagnosis (CAD) system that makes use of advanced deep learning models for automatic image diagnosis and virtually stains MPT images into gold-standard Haematoxylin-Eosin (H&E) images with high sensitivity and specificity has been delivered. Prototype and algorithms have been fully tested on murine models and validation on human models has been (unfortunately) partially achieved.

1.2 Work performed from the beginning of the project to the end of the period covered by the report and main results achieved so far

Medical and commercial needs (WP1) have been identified via questionnaires and personal interviews with external clinicians. Requirements and high-level design have been cyclically revisited and updated as necessary considering unforeseen risks.

The first version of the prototype (WP2 &WP4) was delivered in November 2018. The probe has been designed to be used through the working channel of a colonoscope, so it can be sold separately as an additional advanced component. The set-up of the prototype was performed at CCMIJU facilities, where the animal validation tests have been executed. The results obtained in January 2019 revealed that additional technical development of the probe was required. As one of the major difficulties on this project has been the strong relationship between probe development, image acquisition campaigns and algorithm developments that made project objectives too ambitious, the planning for the next months of the project was reviewed consequently and adapted to support additional probe improvements requesting a 6 months project extension. A new updated probe was delivered in November 2019 and tested again at CCMIJU facilities revealing that the implemented improvements were not providing the expected results on the OCT and MPT image acquisition. Further improvements of the probe have been integrated in the last months of the project and tested during summer 2020. In parallel, a new (confidential) technology that provides enhanced wide-field imaging has been developed and successfully demonstrated within the project. Unfortunately, due to Covid-19 crisis and travel restrictions it has not been possible to make the final tests of the prototype with human samples at hospital facilities.

Generation of new open knowledge has been fully achieved thanks to database management and algorithm implementation (WP3). Various databases have been collected, organized and annotated in the scope of this work package, some for internal use only and three of them made publicly available. A Wide-field Polyp Segmentation algorithm approach, which automatically detects lesions on colonoscopy videos, has been proposed and delivered. Optical biopsy capabilities have been achieved combining various algorithms developments. Advanced strategies based on deep learning able to deal with few samples (a common problem in machine learning), named few-shot learning, have been proposed. Apart from the OCT and MPM classification algorithms and innovative solution that virtually stains MPM images into H&E images has been generated and patent application filled. This innovation aims at facilitating the adoption of advanced imaging techniques by clinicians and ease the learning curve, as it is able to translate unknown images to a known knowledge space by clinicians, as it is the gold-standard H&E.

Fully validation with animal models (WP5) has been achieved through laboratory tests, validation trials, safety tests, etc. during the whole project development, both for the different prototype hardware components and CAD software algorithms. This work has played an important role on the generation of new knowledge and development and validation of optical biopsy algorithms. A database of OCT images using a commercial device has been generated with murine samples. Same specimens have also been used for the development of Colorectal Cancer Molecular Biomarkers based on microRNA analysis. Part of the specimens were healthy animals were hyperplasia has been induced with a model developed and validated in this work package.

Despite the clinical limitations in the last months of the project, various validation actions and generation of new knowledge have been achieved with human samples (WP6). Colonoscopy videos recorded at the Basurto University hospital (BIOEF) have been annotated by project clinicians, generating as a result an openly available database. Additionally, another openly published database of multi-photon microscopy (MPM) images have been acquired at LENS previous selection of samples at Basurto University hospital, where haematoxylin-eosin (H&E) slices have been digitalized and annotated by pathologists. Clinical validation of wide-field polyp segmentation algorithm and optical biopsy algorithms have been achieved performing online surveys and interview with experts and residents.

Ethical implications (WP7) of animal and human models' samples acquisition and validation have been closely monitored during the whole project. The project has defined a regulatory roadmap and data management plan (DMP). Pre-clinical and clinical protocols have been defined and ethical approvals obtained when necessary. Additional ethical approvals for the open publication of the datasets generated at the project have also been managed.

As a result of all this work, different individual results have been made publicly available and presented in a catalogue:

- **Photonics and Optical imaging technologies:**

  1. Endoscopic OCT System

  2. MPT-OCT Endoscopic Probe

  3. MPT Laser

- **CAD Software for colon lesions diagnosis support:**
  - *New Pre-clinical and Clinical knowledge:*

    4. Human Model In-vivo Wide-field Database

    5. Human Model Ex-vivo MPM Database

    6. Murine Model Ex-vivo OCT Database

    7. Induced Colorectal Hyperplastic Murine Model

    8. MicroRNAs as Colorectal Cancer Molecular Biomarkers

  - *Imaging Biomarkers and Tumoral Models:*

    9. Wide-field Polyp Segmentation Algorithm

    Optical Biopsy Algorithms: 10. OCT classifier, 11. MPM classifier, 12. Virtual H&E Stainer, 13. H&E Classifier, 14. Constellation Loss and Few-Shot Learning

With respect to exploitation and dissemination (WP8), the work done and the results achieved in PICCOLO have been shared with the research community and general public through the project website (https://www.piccolo-project.eu) and Twitter (https://twitter.com/piccolo_eu). The summary of publications (https://www.piccolo-project.eu/publications-summary1/) provides an overview of the dissemination activities performed by project partners. News announcing milestones, events and results have been shared on both communication channels (https://www.piccolo-project.eu/news/). A confidential business plan has been elaborated for an endoscope integrating the Photonics and Optical imaging technologies with the CAD Software for colon lesion diagnosis support. Various business models are considered upon commercialization and detailed exploitation plans are defined. Action plans for hardware components and plans to use for software components have been fully defined.

1.3 Progress beyond the state of the art, expected results until the end of the project and potential impacts

Through the MPT laser development and road mapping, M Squared have taken significant steps towards practical deployment of compact titanium sapphire laser technology in clinical environments. Leveraging expertise within the project and a class-leading laser architecture, the use of these powerful lasers in this sector is now a major step closer.

The endoscopic OCT system can take cross-sectional images in 0.3 ms with a depth resolution of 7.5 μm in tissue and has a depth penetration that can visualise both the inner and outer walls of colon tissue. Due to wavelength division components, this can be achieved in combination with other imaging modalities at other wavelengths, thus providing valuable information with motion insensitivity that are needed for a clinical analysis of the nature of the tissue. For a multi-modal endoscopic system, this puts the PICCOLO OCT system at the state-of-the-art, and has done so in a European setting.

A miniaturized scanning system, based on a double-clad fiber and a piezoelectric micro-scanner, has been developed and tested to acquire OCT and multi-photon imaging through the working channel of a colonoscopic system for endoscopic applications. The control and power system, containing the laser sources and the combination system of these, the optics for the fiber coupling, and the electronics relating to both the scan of the distal fiber tip and the detection of signals, has been made in a compact way, so that the device is transportable to allow its application inside the surgical rooms.

Although complete planned clinical validation has not been performed and probe image quality has margin for improvement, important results have been achieved at the project. Considering the very ambitious project objectives, it's important to remark two important achievements.

On the one side, that the delivered probe fits the working channel of a colonoscope and it's no exclusive of a specific device. The colonoscopy industry can benefit from this design solution and offer the optical biopsy probe as an additional component that can be sold separately from the colonoscope, hence maintaining current base retail price. Additional value can be offered if CAD system algorithms are added to the probe purchase. Health systems, clinicians and patients can also benefit from this, as it would make possible to update existing hospital colonoscopes with least monetary investment. Besides, optical biopsy adoption would lead health systems to reduce diagnosis costs, time and patient trauma.

On the other side, the CAD system algorithms. Advanced image processing methods based on deep learning have been implemented on the algorithms. State of the art deep learning techniques have demonstrated to reach precision rates comparable to experts, surpassing them in some cases. Until recently, CAD clinical software was based on classical machine learning techniques that in most cases were not reliable enough to be adopted on the daily clinical routine. With the introduction of deep learning, the market forecast for clinical software is expected to rapidly growth in the short term. In this sense, the resulting metrics of the different algorithms developed in the project, suggests that the realization of the optical biopsy is closer than ever. Besides this, during the PICCOLO project, it has been demonstrated that the future of clinical devices relies on the combination of hardware and software. The virtual staining algorithm approach proposed at the project, which automatically transforms MPT images into gold-standard H&E images, can facilitate the adoption of new imaging techniques by clinicians and at the same time easy the dreaded learning curve.

2. Explanation of the work carried out by the beneficiaries

NOTE: This section summarizes the activities performed on the different work packaged in the reporting period M19-M45.

2.1 WP1 - Clinical and market application driven analysis: clinical, commercial needs and system requirements

2.1.1 Summary

This work package was dedicated to the identification of the clinical and commercial needs, the specification of systems requirements and the definition of the high-level design of the overall solution.

Over the course of this WP, we have obtained the following results:

WP 1 overview

Main results:

1. *Medical & Commercial needs collected and reported*
2. *Functional & non-functional requirements defined using the needs as input*
3. *High Level Design of the PICCOLO endoscope and CAD system defined using requirements and needs as input*

- Medical & Commercial needs, where it was described the needs from a medical and market point of view, to get a product that finds its place on the market.
- Functional and non-functional requirements document, where the technical requirements were described using as input the clinical and commercial needs previously collected.
- High level design (endoscope & CAD system) document, that was being used as a basis of the technical development of the project in WP2 (components), WP3 (CAD system) and WP4 (multi-photonics endoscope).

The execution of this WP implements was an “innovation loop” lifecycle, where several iterations of end-users needs collection and definition of the requirements were performed. During the reporting period, the two final iterations of the cycle have been executed. The needs and requirements where initially collected and defined during the M1-M3 period, then updated and redefined during the M13-M15 period and, finally, reviewed during the M25-M33 period.

2.1.2 Use of resources

Table 1 - Use of resources in WP1

Short name	Used (M19-M45)	Foreseen (M19-M45)	Planned (M1-M45)
TECNALIA	1,38	1,35	3,00
STORZ	2,15	0,90	2,00
L4TNW	0,50	0,90	2,00
TYNDALL	0,00	0,68	1,50
CIT	0,00	0,00	0,00
M2	0,00	0,45	1,00

LENS	3,27	1,80	4,00
CCMIJU	0,42	0,90	2,00
IC	1,00	0,90	2,00
BIOEF	0,86	1,08	2,40
OSAKIDETZA	0,27	0,27	0,60
TOTAL	**9,85**	**9,23**	**20,50**
% spent		**107%**	**48%**

2.2 WP2 - Design and development of photonic sensors components

2.2.1 Summary

This work package has been responsible of delivering the three main physical components that form the PICCOLO photonic system:

- Miniaturized akinetic OCT scanner and probe.
- Miniaturized MPT scanner and probe.
- Fluorescence capable endoscopy system.

During the reporting period, a working version of each component has been delivered and tested on animal tissue, as reported in the WP5 section of this report.

WP 2 overview

Main results:

1. *OCT laser, acquisition cards and lens components upgraded*
2. *OCT images obtained in stand-alone and with PICCOLO probe*
3. *Probe upgraded with new lenses*
4. *MPT Ti:Sapphire laser maintained*
5. *Red flag fluorescence tested successfully*
6. *[Confidencial]*

Disclaimer: This work-package contains confidential and IPR protected work, hence few details can be publicly provided.

2.2.2 Use of resources

Table 2 - Use of resources in WP2

Short name	Used (M19-M45)	Foreseen (M19-M45)	Planned (M1-M45)
TECNALIA	0,00	0,00	0,00
STORZ	19,86	5,72	11,00
L4TNW	2,88	3,64	7,00
TYNDALL	24,02	14,56	28,00
CIT	28,58	9,36	18,00
M2	2,46	6,24	12,00
LENS	8,03	7,75	14,90
CCMIJU	0,00	0,00	0,00
IC	0,00	0,00	0,00
BIOEF	0,00	0,00	0,00
OSAKIDETZA	0,00	0,00	0,00
TOTAL	**85,83**	**47,27**	**90,90**
% spent		**182%**	**94%**

2.3 WP3 - Extraction of imaging biomarkers & Development of CAD module

2.3.1 Summary

The aim of this WP is to provide a clinically validated Computer Aided Diagnosis (CAD) system. The means to achieve this, are the generation of a well annotated database (from animal models-WP5 and human models-WP6) and the implementation of advanced image processing of the multi-source endoscope images (white-light, fluorescence, OCT and MPT signal).

A great amount of the efforts on WP3 during the reporting period (M19-M45) have been focused on acquiring and annotating the required image datasets in collaboration with WP5 and WP6. The implementation of the **algorithms (WP3)** for the automatic extraction of imaging biomarkers and **CAD software** have been running in parallel. As the project prototype integrates two different imaging modalities (wide-field and OCT/MPT), algorithms have been developed separately.

WP 3 overview

Main results:

1. *Open publication of databases:*
   a. *Human Model In-vivo Wide-field database*
   b. *Human Model Ex-vivo MPM database*
   c. *Murine Model Ex-vivo OCT database*
2. *Collection of additional databases for internal use.*
3. *Development of Wide-field Polyp Segmentation algorithm*
4. *Development of Optical Biopsy algorithms:*
   a. *OCT Classifier*
   b. *MPM Classifier*
   c. *Virtual H&E Stainer*
   d. *H&E Classifier*
   e. *Constellation Loss and Few-shot learning*
5. *Development of Computer Aided Diagnosis (CAD) software*

Colonoscopy videos have been recorded and annotated by clinicians at the Basurto University hospital (Spain) with the goal to train and test the wide-field polyp segmentation algorithm implemented by CCMIJU under TECNALIA supervision. Experiments with the wide-field algorithm have been performed using public databases and the PICCOLO database that consist of more than 3,000 annotate images. Details of the algorithms and the database can be found in already published (and ongoing) publications.

Concerning the optical biopsy algorithms, advanced strategies based on the deep learning able to deal with few samples (a common problem in machine learning) have been tested with success and results have been presented at ISBI2019. As probe requires continuous improvement, algorithms have been re-designed to learn from high-quality data and simulate probe quality from a few-shot scheme which has provided outstanding results and it is under patenting process. For the generation of the Human Model Ex-vivo MPM database, BIOEF have provided human samples (previous approval of the hospital ethical committee), stained and provided scanned digital H&E images and diagnosis, LENS has scanned samples with a MPM microscope and TECNALIA developed a co-registering algorithm to co-register MPM with regard to H&E images. This database has been used for the development as testing of various of the optical biopsy algorithms: MPM Classifier, H&E Classifier and Virtual H&E stainer. The Virtual H&E stainer implements latest methods of domain transfers in the state of the art for the automatic conversion of MPM images into H&E images to easy image interpretation by clinicians. A patent has been requested for this innovative solution. Last by not least, murine samples have been scanned at CCMIJU with a commercial OCT device acquired by TECNALIA, who has also post-processed the data for publication and algorithm implementation and BIOEF has performed gold-standard histopathological analysis. An optical biopsy algorithm for automatic diagnosis of OCT images have been developed and tested by TECNALIA.

Finally, A Computer Aided Diagnosis (CAD) software has been developed by STORZ in collaboration with TECNALIA. On the one hand, it obtains the wide-field imaging as input an superimposes the results of the polyp detection algorithm. On the other hand, it obtains the image from the probe and visualizes a virtually stained image and diagnosis result provided by the underlying algorithms.

2.3.2 Use of resources

Table 3 - Use of resources in WP3

Short name	Used (M19-M45)	Foreseen (M19-M45)	Planned (M1-M45)
TECNALIA	46,38	42,33	51,00
STORZ	5,45	5,81	7,00
L4TNW	0,50	0,83	1,00
TYNDALL	0,00	0,00	0,00
CIT	0,00	0,00	0,00
M2	0,00	0,00	0,00
LENS	15,14	20,34	24,50
CCMIJU	6,59	6,64	8,00
IC	3,00	3,32	4,00
BIOEF	3,92	3,74	4,50
OSAKIDETZA	1,36	1,25	1,50
TOTAL	**82,34**	**84,25**	**101,50**
% spent		**98%**	**81%**

2.4 WP4 - Design, development and integration: multi-source endoscope

2.4.1 Summary

WP4 has been focused on the design, development and integration of a fully functional engineered prototype, including both MPT and OCT techniques. During this WP, the prototype is tested from optical, mechanical and software sides. During the period under review, the prototype version of the PICCOLO device was transformed into a portable device, creating the mechanical housing of the system within which the entire optical and electronic system was positioned. Furthermore, the tests of the system highlighted the need to replace some opto-mechanical components and to redesign some parts to improve system performance.

WP 4 overview

***Main results**:*

1 Integration of the PICCOLO prototype as a portable device

2 Realization of probes with specific GRIN lenses for both techniques

3 Realization of a probe based on fiber bundle

4 Tests on probe insertion in the colonoscope working channel

5 Development and improvement of the software

Disclaimer: This work-package contains confidential and IPR protected work, hence few details can be publicly provided.

2.4.2 Use of resources

Table 4 - Use of resources in WP4

Short name	Used (M19-M45)	Foreseen (M19-M45)	Planned (M1-M45)
TECNALIA	1,25	6,16	8,00
STORZ	0,38	5,39	7,00
L4TNW	27,60	31,57	41,00
TYNDALL	9,01	7,70	10,00
CIT	2,02	1,54	2,00
M2	0,00	4,62	6,00
LENS	10,08	11,70	15,20
CCMIJU	0,00	0,00	0,00
IC	0,00	0,00	0,00
BIOEF	0,00	0,00	0,00
OSAKIDETZA	0,00	0,00	0,00
TOTAL	**50,34**	**68,68**	**89,20**
% spent		**73%**	**56%**

2.5 WP5 - Validation on Animal Models

2.5.1 Summary

> ***WP5 overview***
>
> ***Main results:***
>
> 1. *Creation of a hyperplastic model of growth in colon by laparotomy with sutures on murine model*
> 2. *Laboratory tests*
>   a. *Validation of most promising fluorescent marker is a suitable red flag staining option for dysplastic mucosa to be used with fluorescence technologies.*
>   b. *Collection of hyperspectral (VIS/NIR) and RGB images of healthy and neoplastic murine tissue.*
> 3. *Definition and validation of a protocol for tissue autofluorescence preservation for later acquisition with MPT and OCT.*
> 4. *System validation on animal models*
>   a. *Several tests with MPT and OCT technologies on ex-vivo and in-vivo rat samples to distinguish between healthy and unhealthy tissue*
>   b. *Acquisition of the database of OCT images from ex-vivo murine healthy tissue, hyperplasic and neoplastic polyps*
> 5. *Safety tests to evaluate the photo-toxicity of the laser light of the MPT system*
> 6. *Proposal of microRNAs tests to obtain novel molecular biomarkers of colorectal cancer with blood and plasma extractions from murine model*

In the second and final reporting period, different tests have been carried out with the different versions of the PICCOLO components under laboratory conditions corresponding to the task 5.2 “Laboratory tests”: a) red flag fluorescence technologies were tested with different fluorescent markers, with only one being satisfactory; b) a big collection of hyperspectral and RGB images were obtained; c) different tests for improvements of MPT and OCT photonic components; d) a protocol for tissue autofluorescence preservation has been achieved with successful results for MPT and OCT acquisitions. Regarding task 5.3, two set of tests for the system validation on animal models have been carried out with the PICCOLO prototype and other systems: a) Red Flag Fluorescence Technologies were tested in depth; b) MPT tests were performed on ex-vivo and in-vivo rat samples, including safety trials performed on colonic tissue from rabbits to evaluate the photo-toxicity of the laser light; c) OCT tests with stand-alone system using a microscope objective and the PICCOLO probe to distinguish between healthy and unhealthy tissue; d) tests with commercial Thorlabs OCT to achieve a broad database of OCT images from ex-vivo murine model for the application of a deep learning-based algorithm for automatic image classification; e) a hyperplastic model of growth in colon has been created by laparotomy with sutures on murine model; f) tests with microRNAs to obtain novel molecular biomarkers of colorectal cancer with blood and plasma extractions from murine model.

2.5.2 Use of resources

Table 5 - Use of resources in WP5

Short name	Used (M19-M45)	Foreseen (M19-M45)	Planned (M1-M45)
TECNALIA	6,00	6,39	9,00
STORZ	0,00	0,00	0,00
L4TNW	7,92	7,10	10,00

TYNDALL	1,29	0,71	1,00
CIT	0,50	0,36	0,50
M2	0,00	0,00	0,00
LENS	10,64	8,52	12,00
CCMIJU	31,56	29,11	41,00
IC	4,15	4,26	6,00
BIOEF	6,85	5,54	7,80
OSAKIDETZA	0,30	0,14	0,20
TOTAL	**69,21**	**62,13**	87,50
% spent		**73%**	**79%**

2.6 WP6 - Validation on Human Models

2.6.1 Summary

WP6 has been responsible for defining the pre-clinical trials on human models, which will be undertaken as part of the PICCOLO project. It is also responsible for producing the report of the results of the human model trials. As the work package lead and the clinical partner within the PICCOLO project, Imperial College (IC) has also been responsible for providing clinical input and opinion to other work packages throughout the project.

WP 6 overview

***Main results**:*

1 First version of the human tissue validation plan

a Human trial protocols

b Data acquisition plans

2 Early clinical validation of wide-field polyp detection algorithm

3 First assessment of clinical characteristics of MPM images

4 Clinical evaluation of 'virtual staining' algorithm for MPM to H+E images

5 First successful analysis of molecular imaging agent

The first period of the project was spent defining the clinical needs of the planned multimodal endoscope, including the physical function of the endoscope, the processing and operating needs. We liaised with the other work parties to guide and define the required optical parameters to answer the clinical questions posed within the project brief.

Part of this work included thorough review of the existing literature and research within this field, and assessment of the imaging capabilities of competing and complementary technologies, including Optical Coherence Tomography, Multiphoton Microscopy, Confocal Laser Endomicroscopy, Raman Spectrography, and Molecular Labelled Imaging. This is publically referenced at https://www.piccolo-project.eu/publications-summary1/ and informs the development of the PICCOLO endoscope.

The second period of the project has included local preparation for receiving the PICCOLO prototype device, and the plans to conduct the first in-human tissue studies. This has included the institutional ethical approval, data protection, and safety considerations, which have been prepared and are ready to progress at such a time when the PICCOLO project reaches this stage.

The third period of the project has been the final preparation for conducting human tissue studies, including the preparation of the Human Tissue Validation Plan (D6.1). This stage was delayed unavoidably by difficulties in presenting the functional version of the PICCOLO endoscope, and then further by the global disruption to both clinical research activity, and endoscopy activity.

To mitigate the unavoidable delays, further avenues of study were explored in conjunction with other work parties, including evaluation of human tissues by means of MPM imaging, and comparison with traditional microscopy. IC also provided the histological analysis and support for processing of labelled samples to evaluate the selected molecular imaging technology.

2.6.2 Use of resources

Table 6 - Use of resources in WP6

Short name	Used (M19-M45)	Foreseen (M19-M45)	Planned (M1-M45)
TECNALIA	8,10	9,00	9,00
STORZ	0,00	0,00	0,00
L4TNW	0,00	6,00	6,00
TYNDALL	0,00	0,00	0,00
CIT	0,00	0,00	0,00
M2	0,00	0,00	0,00
LENS	5,99	6,00	6,00
CCMIJU	2,99	4,00	4,00
IC	15,35	24,00	24,00
BIOEF	6,23	5,65	5,65
OSAKIDETZA	2,89	2,35	2,35
TOTAL	**41,55**	**57,00**	**57,00**
% spent		**73%**	**73%**

2.7 WP7 - Ethical and Regulatory Strategies

2.7.1 Summary

> ***WP 7 overview***
>
> ***Main results:***
>
> *1. Pre-clinical and clinical protocols updates.*
>
> *2. Maintaining and Obtaining new ethical approvals (for research with animals and human samples).*
>
> *3. Regulatory Roadmap for the project Update.*
>
> *4. Development of the Data Management Plan (DMP) for the project including the Risk Assessment report.*
>
> *5. Ethical approvals for Biobank sample use.*
>
> *6. Ethical approvals for databases publication.*

This work package has focused on the ethical, legal, regulatory and safety issues associated to the development of the PICCOLO diagnosis medical device that will accelerate the road to market process in an ethical and safe way.

During the first 18 months of the project, important achievements were made in relation with WP7: The pre-clinical and clinical protocols were defined to be carried out in the validation process of the PICCOLO medical device. Furthermore, all ethical approvals and relevant documents were obtained in the corresponding clinical institution (IC, BIOEF and CCMIJU) to get access to the biological material that will be used in both the clinical setting with human patients and the experimental animals (pre-clinical studies). During months 19 to 30, pre-clinical protocols have been modified according to new Gannt.

During the last 15 months of the project, the final version of the Data Management Plan (DMP) has been performed, including the risk assessment report. Furthermore, all the ethical documents required for the publication of the databases have been drawn up and presented to the relevant ethics committees. In the same way, these databases will be published, maintained and managed from the page of the Basque Biobank, within BIOEF. Thus, from BIOEF, we have participated in the drafting of relevant publications regarding them.

In cases where samples from the Biobank have been needed, these samples have been transferred, as well as the ethical needs for it, managed.

2.7.2 Use of resources

Table 7 - Use of resources in WP7

Short name	Used (M19-M45)	Foreseen (M19-M45)	Planned (M1-M45)
TECNALIA	0,00	0,00	0,00
STORZ	0,00	4,80	8,00
L4TNW	0,30	1,20	2,00
TYNDALL	0,00	0,00	0,00
CIT	0,00	0,00	0,00
M2	0,00	1,20	2,00

LENS	0,00	0,00	0,00
CCMIJU	3,76	3,60	6,00
IC	1,00	3,60	6,00
BIOEF	3,55	3,60	6,00
OSAKIDETZA	0,77	0,60	1,00
TOTAL	**9,38**	**18,60**	**31,00**
% spent		**50%**	**30%**

2.8 WP8 - Exploitation & Dissemination

2.8.1 Summary

WP8 aimed for the Exploitation & Dissemination of the PICCOLO project results and included the continuous observation of competitors and scientific technology progress outside the project.

The first period aim of WP8 was building the infrastructure for a successful dissemination. The achieved results were building a marketing infrastructure with a webpage http://www.piccolo-project.eu/ and a twitter account https://twitter.com/piccolo_eu. Further dissemination activities included creating marketing material (patient's leaflets) and holding public presentations to inform the public about PICCOLO's aims. All activities intended to form a contact point to the public as well as the scientific community. The emphasize of the months M19-M45 was focusing on further steps to explore the project results of PICCOLO.

> ***WP8 overview***
>
> ***Main results:***
>
> *1 Increased dissemination activities: leaflets, project promotional video, results catalogue, results short videos, etc.*
>
> *2 3rd and final version of PEDR*
>
> *3 Report of State of the art leading to a patentability and FTO*
>
> *4 First version and final version of the Business Plan*
>
> *5 Clinical workshops and training sessions performed*
>
> *6 Final version of Technology watch & Competitive intelligence report*

The public dissemination of results was generated for the general public, fellow scientists and clinicians by presentations at scientific conferences, publishing on the project website and on Twitter. Dissemination and communication activity have significantly increased (specially on the website and twitter) following the recommendation of the 2nd project review. Leaflets were designed for patients, clinicians and the general public. In addition, a brochure highlighting the main results of the project has been designed, and these results have been converted to videos that have been published on the project website and twitter and easily shared by partners on events/meetings. The 3rd and final version of the Plan for the Exploitation and Dissemination of Results (PEDR) was delivered representing the current status of exploitation, dissemination and communication actions conducted.

Several training sessions and clinical workshops have been performed as planned while others had to be cancelled due to the device not being ready or the Covid-19 crisis stopping routine work.

PICCOLO partners elaborated a business plan for the final colonoscope solution developed in the project, selecting the most promising exploitation scenario, updating the IPR management and analysing the latest partners' expectations and roles. Action plans were developed for the most mature technologies, as well as plans to use for the less commercially useable results.

Patentability and IPR protection opportunities were also studied, identifying possible patents that may affect technological developments and performing a freedom to operate (FTO) analysis for the main project results.

In addition, the final version of the Technology watch & Competitive intelligence report was delivered comprising state-of-the-art technologies provided by competitors, research prototypes and patents. As in the previous report, to our knowledge, no equivalent product development has been observed which endangers the PICCOLO product aim for an onsite analysis of colorectal polyps in colonoscopy. Nevertheless, it has to be mentioned that the large number of new evolving technologies and research prototypes should be monitored closely while developing the final PICCOLO endoscope and probes.

2.8.2 Use of resources

Table 8 - Use of resources in WP8

Short name	Used (M19-M45)	Foreseen (M19-M45)	Planned (M1-M45)
TECNALIA	8,87	7,20	12,00
STORZ	12,25	9,00	15,00
L4TNW	1,50	2,40	4,00
TYNDALL	2,00	2,10	3,50
CIT	0,50	0,30	0,50
M2	0,00	1,80	3,00
LENS	6,57	4,20	7,00
CCMIJU	8,92	6,00	10,00
IC	1,00	4,20	7,00
BIOEF	0,81	0,60	1,00
OSAKIDETZA	1,92	1,50	2,50
TOTAL	**44,34**	**39,30**	**65,50**
% spent		**113%**	**68%**

2.9 WP9 - Management & Coordination

2.9.1 Summary

This work package is focused on the coordination of the project at internal, financial and strategic levels, in order to guarantee a successful development of the project, meeting the scientific and technical objectives accordingly to the established time schedule and budget, as well as ensuring a fluent communication between all the project partners.

During the M19-M45 period, project continued developing the different WPs and components. Intrinsic difficulties and strong correlation among the different project tasks, as well as unforeseen risks (as the Covid-19 global crisis), made necessary to take countermeasures for the benefit of the project.

WP 9 overview

***Main results**:*

1. *Organization of four GA and EB consortium meetings.*
2. *Continuous reporting through monthly online project monitoring meetings.*
3. *Establishment of Post-project impact follow-up Committee (PPIF) and meetings organization.*
4. *Management of project risks and project deviations.*
5. *Management of project amendments.*
6. *Validation of project ethical and legal actions by external ethical committee.*
7. *Quality assurance of project deliverables and dissemination material.*

2.9.2 Use of resources

Table 9 - Use of resources in WP9

Short name	Used (M19-M45)	Foreseen (M19-M45)	Planned (M1-M45)
TECNALIA	14,10	10,80	18,00
STORZ	2,26	1,20	2,00
L4TNW	0,91	1,20	2,00
TYNDALL	1,48	1,20	2,00
CIT	0,00	0,00	0,00
M2	0,69	1,20	2,00
LENS	0,85	0,60	1,00
CCMIJU	1,76	1,80	3,00
IC	0,50	1,20	2,00
BIOEF	2,05	1,50	2,50
OSAKIDETZA	0,00	0,00	0,00
TOTAL	**24,60**	**20,70**	**34,50**
% spent		**119%**	**71%**

3. Deviations from Annex I

3.1 Tasks

There are no significant deviations in the tasks that affect negatively to the outcome on the project from current DoA (AMD-732111-23).

3.2 Use of resources

3.2.1 Reporting period M19-M45

According to the current DoA (AMD-732111-23), there are not important deviations in the Use of the Resources concerning Personnel and other direct costs. **In this Period of the project (M19-M45), the percentage used is around 69%**, that corresponds with the work made. **For the whole project we have already spent the 105% of the total budget.**

There are some differences on WP2 and WP4 foreseen and declared effort. Being bigger than expected in WP2 and lower in WP4. The reason of this is that these two work-packages are very tight related, and in some cases it has been difficult for partners to distinguish/separate the actions performed at the different tasks, resulting on more effort reported in WP2. Besides, as previously reported and agreed with project officer and reviewers, extra-effort had to be done in WP2 in order to solve problems with the photonics components, specially on the OCT system, and efforts and costs had to be reallocated.

Concerning WP6, not all the clinical activities planned at the project have been achieved, resulting in less effort dedicated in this work package. The reason for this, as previously reported in this document, is that some of the evaluation/validation activities planned in clinical settings could not be performed due to hospital access restrictions and less clinicians availability during the Covid-19 healthy crisis.

Finally, all WP7 activities have been successfully accomplished with less effort that the initially planned.

3.2.1.1 Personnel effort

Table 10 summarizes the effort of each participant in this period and compares it with the foreseen data for the whole duration of the project and the estimated progress (based on time spent, %). **72% of PMs have been declared in this period**.

Table 10 - Partner / Effort (M19-M45)

PARTNER	Personnel PMs		% of total PMs requested
	Declared [1]	Foreseen [2]	
TECNALIA	86,08	110,00	78,25%
STORZ	42,35	52,00	81,44%
L4TNW	42,11	75,00	56,15%
TYNDALL	37,80	46,00	82,17%
CIT	31,60	21,00	150,48%

M2	3,15	26,00	12,12%
LENS	60,57	84,60	71,60%
CCMIJU	56,00	74,00	75,68%
IC	26,00	51,00	50,98%
BIOEF	24,27	29,85	81,31%
OSAKIDETZA	7,51	8,15	92,15%
TOTAL	**417,44**	**577,6**	**72,27%**
real spent % M19-M45	**72%**		

Table 11 summarizes the effort of each participant in each of the Work Packages and compares it with the foreseen data in this period. The foreseen data is based in the active months in this 2nd period (M19-M45) compared with the total months of the WP. The real % spent in each WP during the 2nd period is also included.

Table 11 – Partner effort per WP (M19-M45)

PARTNER / EFFORT	WP1		WP2		WP3		WP4		WP5	
	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]
TECNALIA	1,38	1,35	0,00	0,00	46,38	42,33	1,25	6,16	6,00	6,39
STORZ	2,15	0,90	19,86	5,72	5,45	5,81	0,38	5,39	0,00	0,00
L4TNW	0,50	0,90	2,88	3,64	0,50	0,83	27,60	31,57	7,92	7,10
TYNDALL	0,00	0,68	24,02	14,56	0,00	0,00	9,01	7,70	1,29	0,71
CIT	0,00	0,00	28,58	9,36	0,00	0,00	2,02	1,54	0,50	0,36
M2	0,00	0,45	2,46	6,24	0,00	0,00	0,00	4,62	0,00	0,00
LENS	3,27	1,80	8,03	7,75	15,14	20,34	10,08	11,70	10,64	8,52
CCMIJU	0,42	0,90	0,00	0,00	6,59	6,64	0,00	0,00	31,56	29,11
IC	1,00	0,90	0,00	0,00	3,00	3,32	0,00	0,00	4,15	4,26
BIOEF	0,86	1,08	0,00	0,00	3,92	3,74	0,00	0,00	6,85	5,54
OSAKIDETZA	0,27	0,27	0,00	0,00	1,36	1,25	0,00	0,00	0,30	0,14
TOTAL Person/Months	**9,85**	**9,23**	**85,83**	**47,27**	**82,34**	**84,25**	**50,34**	**68,68**	**69,21**	**62,13**
estimated progress M19-M45 (based on time spent) (%)		**45%**		**52%**		**83%**		**77%**		**71%**
real spent % M19-M45	**107%**		**182%**		**98%**		**73%**		**111%**	

Declared [1] effort and costs declared in the project

Foreseen [2] foreseen data for M19-M45

WP6		WP7		WP8		WP9		WP10		TOTAL		% of PMs
Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	
8,10	9,00	0,00	0,00	8,87	7,20	14,10	10,80	0,00	0,00	86,08	83,23	103,42%
0,00	0,00	0,00	4,80	12,25	9,00	2,26	1,20	0,00	0,00	42,35	32,82	129,04%
0,00	6,00	0,30	1,20	1,50	2,40	0,91	1,20	0,00	0,00	42,11	54,84	76,79%
0,00	0,00	0,00	0,00	2,00	2,10	1,48	1,20	0,00	0,00	37,80	26,95	140,29%
0,00	0,00	0,00	0,00	0,50	0,30	0,00	0,00	0,00	0,00	31,60	11,56	273,47%
0,00	0,00	0,00	1,20	0,00	1,80	0,69	1,20	0,00	0,00	3,15	15,51	20,31%
5,99	6,00	0,00	0,00	6,57	4,20	0,85	0,60	0,00	0,00	60,57	60,91	99,45%
2,99	4,00	3,76	3,60	8,92	6,00	1,76	1,80	0,00	0,00	56,00	52,05	107,59%
15,35	24,00	1,00	3,60	1,00	4,20	0,50	1,20	0,00	0,00	26,00	41,48	62,68%
6,23	5,65	3,55	3,60	0,81	0,60	2,05	1,50	0,00	0,00	24,27	21,70	111,83%
2,89	2,35	0,77	0,60	1,92	1,50	0,00	0,00	0,00	0,00	7,51	6,11	122,97%
41,55	**57,00**	**9,38**	**18,60**	**44,34**	**39,30**	**24,60**	**20,70**	**0,00**	**0,00**	**417,44**	**407,15**	**102,53%**
	100%		**60%**		**60%**		**60%**				**72%**	
73%		**50%**		**113%**		**119%**				**103%**		

Declared [1] effort and costs declared in the project

Foreseen [2] foreseen data for M19-M45

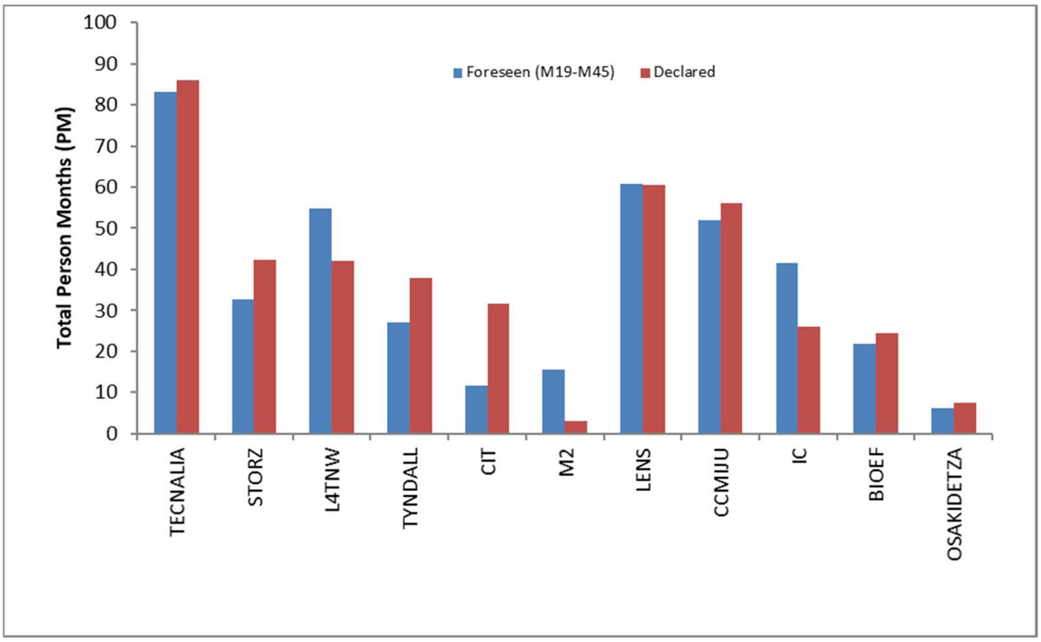

Figure 1 - M19-M45 effort per partner

3.2.1.2 Direct costs

Partners request table summarizes the declared costs of each participant in this period and compares it with the foreseen data for the whole duration of the project.

Table 12 - Partners request from M19 to M45

PARTNER	Personnel costs		Subcontracting		Other direct costs		Indirect costs		TOTAL		EU Contribution		% of total foreseen costs requested
	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Requested [1]	Foreseen [2]	
TECNALIA	392.279,29	474.430,00	0,00	0,00	36.458,89	72.370,00	107.184,55	136.700,00	535.922,73	683.500,00	535.922,73	683.500,00	78,41%
STORZ	338.453,28	260.000,00	0,00	0,00	126.264,07	134.000,00	116.179,34	98.500,00	580.896,69	492.500,00	580.896,69	492.500,00	117,95%
L4TNW	193.422,65	300.000,00	0,00	0,00	31.988,25	101.000,00	56.352,73	100.250,00	281.763,63	501.250,00	281.763,63	501.250,00	56,21%
TYNDALL	125.609,10	131.830,00	0,00	0,00	47.925,20	112.704,00	43.383,58	61.133,50	216.917,88	305.667,50	216.917,88	305.667,50	70,97%
CIT	114.690,15	105.840,00	0,00	0,00	14.093,50	34.696,00	32.195,91	35.134,00	160.979,56	175.670,00	160.979,56	175.670,00	91,64%
M2	27.961,00	169.000,00	0,00	0,00	4.118,27	118.000,00	8.019,82	71.750,00	40.099,09	358.750,00	40.099,09	358.750,00	11,18%
LENS	136.067,08	196.000,00	0,00	0,00	62.840,27	93.200,00	49.726,84	72.300,00	248.634,19	361.500,00	248.634,19	361.500,00	68,78%
CCMIJU	145.301,02	229.400,00	0,00	0,00	66.420,17	122.960,00	52.930,30	88.090,00	264.651,49	440.450,00	264.651,49	440.450,00	60,09%
IC	152.086,47	246.461,00	0,00	0,00	11.727,13	40.133,00	40.953,40	71.648,50	204.767,00	358.242,50	204.767,00	358.242,50	57,16%
BIOEF	102.559,47	132.270,00	0,00	0,00	12.947,94	66.100,00	28.876,85	49.592,50	144.384,26	247.962,50	144.384,26	247.962,50	58,23%
OSAKIDETZA	57.247,48	57.730,00	0,00	0,00	0,00	0,00	14.311,87	14.432,50	71.559,35	72.162,50	71.559,35	72.162,50	99,16%
TOTAL	**1.785.676,99**	**2.302.961,00**	**0,00**	**0,00**	**414.783,69**	**895.163,00**	**550.115,17**	**799.531,00**	**2.750.575,85**	**3.997.655,00**	**2.750.575,85**	**3.997.655,00**	**68,80%**
real spent % M19-M45	**78%**				**46%**		**69%**		**69%**		**69%**		

Declared [1] effort and costs in this period

Foreseen [2] foreseen data for the whole duration of the project

The comparison is also graphically shown in the following diagrams:

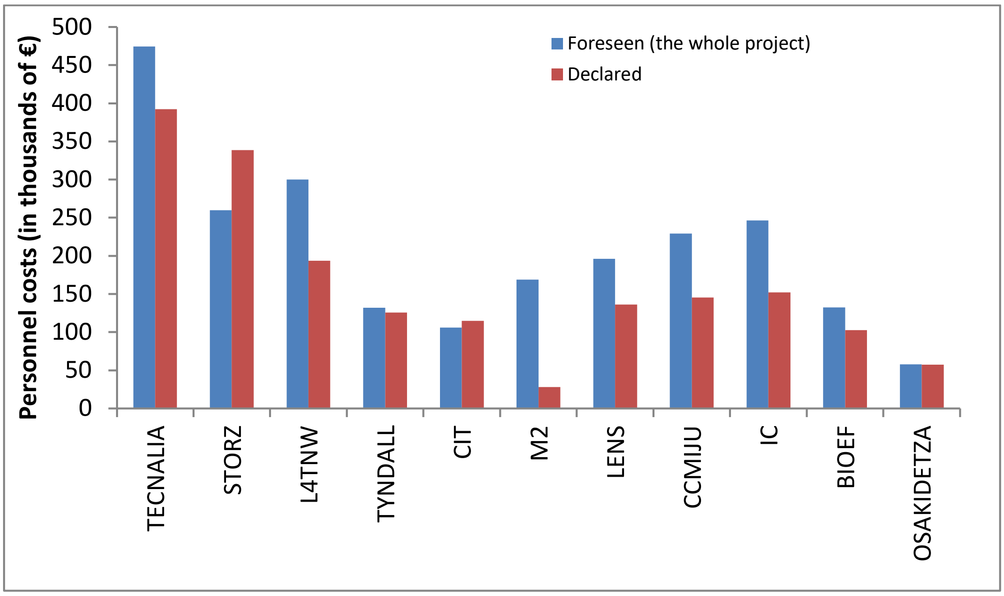

Figure 2 - Personnel costs for M19-M45

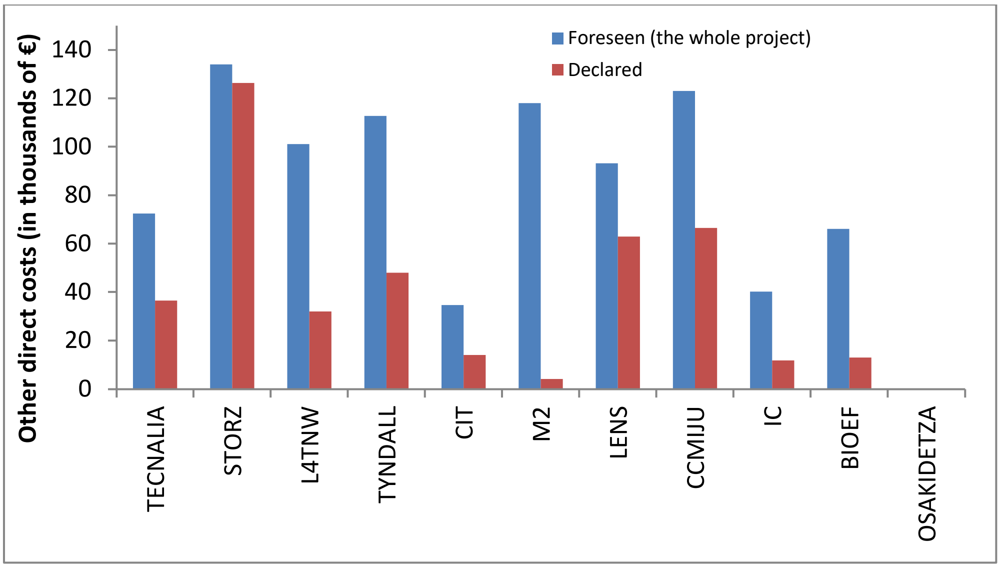

Figure 3 - Other direct costs for M19-M45

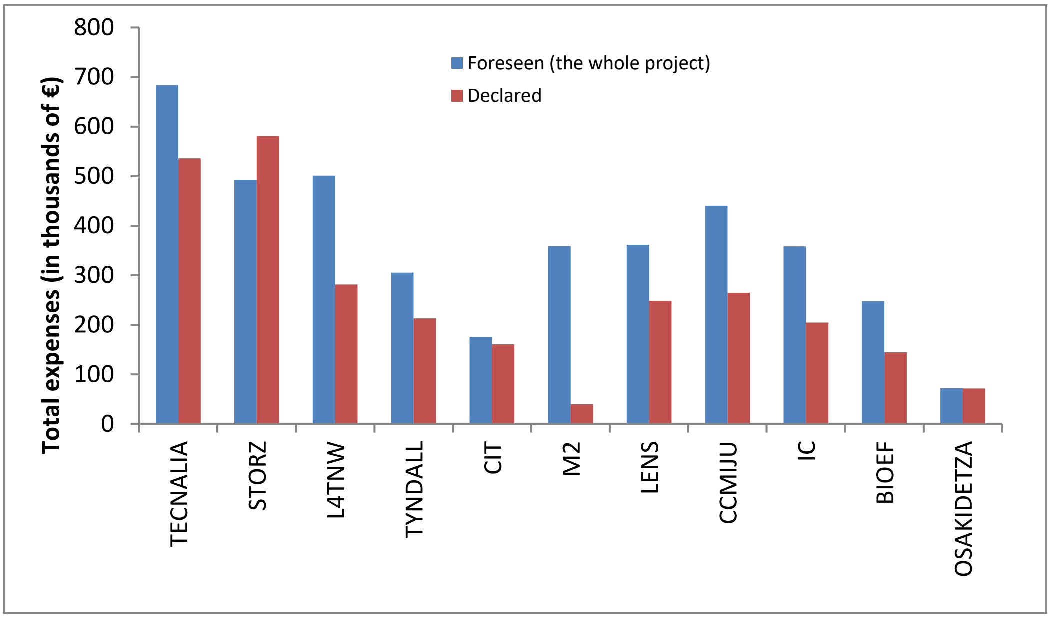

Figure 4 - Total expenses for M19-M45

3.2.2 Overall project summary M1-M45

Table 13 – M1-M45 costs per categories

Resources Monitoring Table								
Contract N°:	732111		Acronym:		Period:			Date:
PARTICIPANTS	UNIT (*PERSON-MONTHS or EUROS*)	TYPE of EXPENDITURE	PLANNED	L EXPENDITURE			Pct. Spent	REMAINING RESOURCES
				Adjustment	Period 2 01/07/2018 - 30/09/2020	Total	TOTAL	
			e	c1	d1	e1	a1+b1+c1+d1/e	e-e1
Totals	*P-M*	Work Package 1	20,50	0,00	9,85	20,45	100%	0,05
	P-M	Work Package 2	90,90	0,00	85,83	139,79	154%	-48,89
	P-M	Work Package 3	101,50	0,24	82,34	113,97	112%	-12,47
	P-M	Work Package 4	89,20	0,00	50,34	100,11	112%	-10,91
	P-M	Work Package 5	87,50	0,25	69,21	101,41	116%	-13,91
	P-M	Work Package 6	57,00	0,00	41,55	43,95	77%	13,05
	P-M	Work Package 7	31,00	0,00	9,38	20,01	65%	10,99
	P-M	Work Package 8	65,50	0,00	44,34	63,44	97%	2,06
	P-M	Work Package 9	34,50	0,00	24,60	38,03	110%	-3,53
	P-M	Work Package 10	0,00	0,00	0,00	0,00	0%	0,00
	P-M	*Total*	577,60	0,49	417,44	641,16	111%	-63,56
	Euros	Personnel costs	2.302.961,00	11.201,42	1.785.676,99	2.717.302,50	118%	-414.341,50
	Euros	Subcontracting	0,00	0,00	0,00	0,00	0%	0,00
	Euros	Other direct costs	895.163,00	-5.820,80	414.783,69	652.132,29	73%	243.030,71
	Euros	Indirect Costs	799.531,00	1.345,16	550.115,17	842.358,70	105%	-42.827,70
	Euros	Total Costs	3.997.655,00	6.725,78	2.750.575,85	4.211.793,49	105%	-214.138,49
	Euros	Requested EU funding	3.997.655,00	6.725,78	2.750.575,85	4.211.793,49	105%	-214.138,49

Partners request table summarizes the declared costs of each participant in the project (M1-M30) and compares it with the foreseen data for the whole duration of the project (M1-M45)

Table 14 – M1-M45 totals PMs declared

PARTNERS	WP1		WP2		WP3		WP4		WP5		WP6		WP7		WP8		WP9	
	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]	Declared [1]	Foreseen [2]
TECNALIA	3,00	3,00	0,00	0,00	58,00	51,00	8,88	8,00	9,01	9,00	9,00	9,00	0,00	0,00	14,15	12,00	22,24	18,00
STORZ	3,30	2,00	24,04	11,00	5,91	7,00	0,88	7,00	0,02	0,00	0,00	0,00	1,02	8,00	16,64	15,00	2,61	2,00
L4TNW	2,00	2,00	8,38	7,00	0,50	1,00	51,40	41,00	10,10	10,00	0,00	6,00	2,00	2,00	2,98	4,00	2,00	2,00
TYNDALL	1,25	1,50	34,00	28,00	0,00	0,00	13,00	10,00	1,29	1,00	0,00	0,00	0,00	0,00	3,80	3,50	1,78	2,00
CIT	0,00	0,00	32,01	18,00	0,00	0,00	2,02	2,00	0,50	0,50	0,00	0,00	0,00	0,00	0,50	0,50	0,00	0,00
M2	0,00	1,00	26,46	12,00	0,00	0,00	7,84	6,00	0,00	0,00	0,00	0,00	0,00	2,00	0,00	3,00	1,69	2,00
LENS	4,00	4,00	14,90	14,90	25,86	24,50	15,20	15,20	12,86	12,00	5,99	6,00	0,00	0,00	6,75	7,00	1,00	1,00
CCMIJU	2,15	2,00	0,00	0,00	12,41	8,00	0,00	0,00	53,24	41,00	2,99	4,00	7,49	6,00	14,19	10,00	3,66	3,00
IC	2,05	2,00	0,00	0,00	4,16	4,00	0,89	0,00	5,33	6,00	16,85	24,00	1,00	6,00	1,00	7,00	0,50	2,00
BIOEF	2,10	2,40	0,00	0,00	5,14	4,50	0,00	0,00	8,58	7,80	6,23	5,65	7,35	6,00	1,25	1,00	2,49	2,50
OSAKIDETZA	0,60	0,60	0,00	0,00	1,99	1,50	0,00	0,00	0,48	0,20	2,89	2,35	1,15	1,00	2,18	2,50	0,06	0,00
TOTAL	20,45	20,50	139,79	90,90	113,97	101,50	100,11	89,20	101,41	87,50	43,95	57,00	20,01	31,00	63,44	65,50	38,03	34,50
% Spent		100%		154%		112%		112%		116%		77%		65%		97%		110%

Declared [1] effort and costs declared in the project

Foreseen [2] foreseen data for the whole duration of the project

PARTNERS	Personnel PMs		% of PMs declared
	Declared [1]	Foreseen [2]	
TECNALIA	124,28	110,00	112,98%
STORZ	54,42	52,00	104,65%
L4TNW	79,36	75,00	105,81%
TYNDALL	55,12	46,00	119,83%
CIT	35,03	21,00	166,81%
M2	35,99	26,00	138,42%
LENS	86,56	84,60	102,32%
CCMIJU	96,13	74,00	129,91%
IC	31,78	51,00	62,31%
BIOEF	33,14	29,85	111,02%
OSAKIDETZA	9,35	8,15	114,72%
TOTAL	641,16	577,60	111,00%

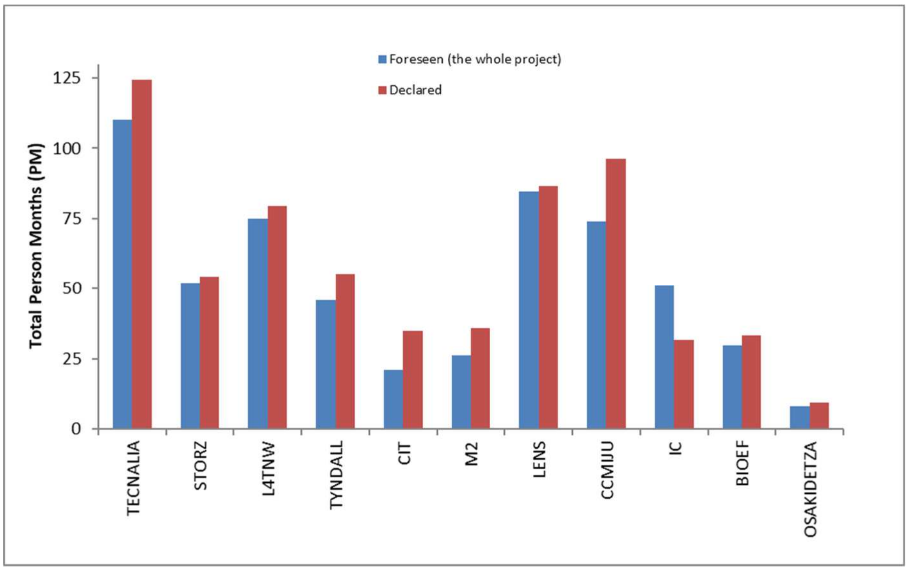

Figure 5 – Comparison of PM declared versus foreseen per partner, M1-M45

Table 15 – Summary of PM planned and declared per work package, M1-M45

	Planned Effort M1-M45	Actual Effort M1-M45	% Effort M1-M45
WP1 (M1-M33)	20,50	20,45	99,76%
WP2 (M3-M34)	90,90	139,79	153,78%
WP3 (M13-M43)	101,50	113,97	112,29%
WP4 (M10-M45)	89,20	100,11	112,23%
WP5 (M7-M45)	87,50	101,41	115,90%
WP6 (M29-M45)	57,00	43,95	77,11%
WP7 (M1-M45)	31,00	20,01	64,55%
WP8 (M1-M45)	65,50	63,44	96,85%
WP9 (M1-M45)	34,50	38,03	110,23%
TOTAL	577,60	641,16	111,00%

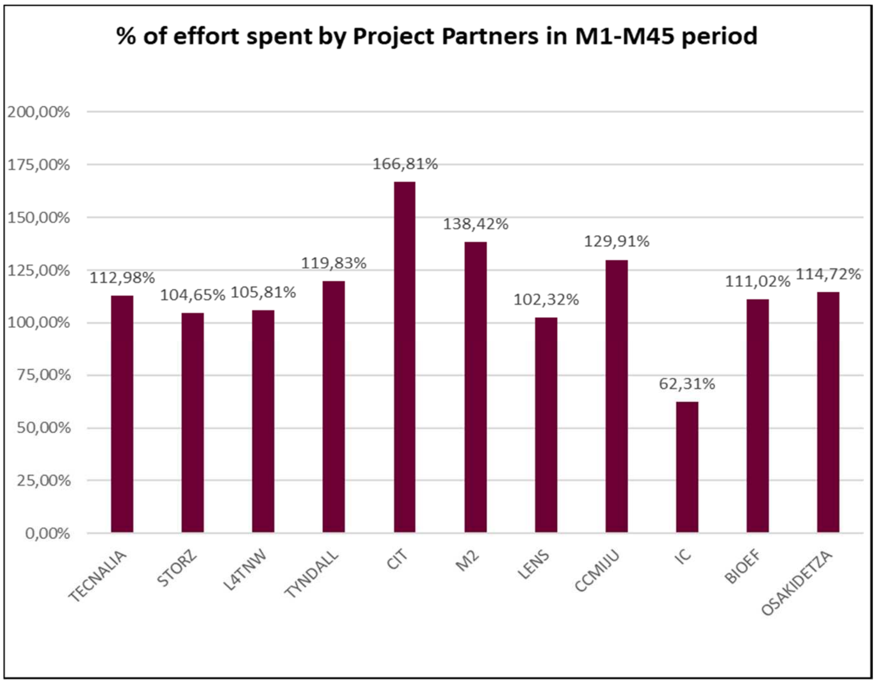

Figure 6 - % effort spent by project partners, M1-M45

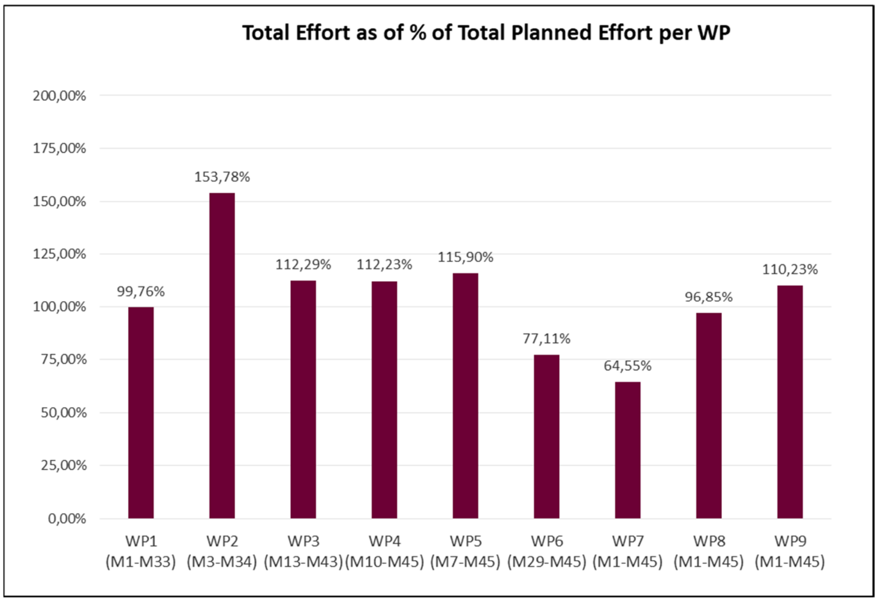

Figure 7 – Total effort as of % of total planned effort per work package, M1-M45

Table 16 – M1-M45 costs per categories

PARTNER	Personnel costs		Subcontracting		Other direct costs		Indirect costs		TOTAL		EU Contribution		% of total foreseen costs spent
	Declared 1	Foreseen 2	Declared 1	Foreseen 2	Declared 1	Foreseen 2	Declared 1	Foreseen 2	Declared 1	Foreseen 2	Requested 1	Foreseen 2	
TECNALIA	556.332,86	474.430,00	0,00	0,00	56.781,69	72.370,00	153.278,64	136.700,00	766.393,19	683.500,00	766.393,19	683.500,00	112,13%
STORZ	423.512,77	260.000,00	0,00	0,00	146.599,46	134.000,00	142.528,06	98.500,00	712.640,29	492.500,00	712.640,29	492.500,00	144,70%
L4TNW	342.436,42	300.000,00	0,00	0,00	58.574,73	101.000,00	100.252,79	100.250,00	501.263,94	501.250,00	501.263,94	501.250,00	100,00%
TYNDALL	193.660,78	131.830,00	0,00	0,00	69.849,21	112.704,00	65.877,50	61.133,50	329.387,49	305.667,50	329.387,49	305.667,50	107,76%
CIT	126.029,15	105.840,00	0,00	0,00	15.564,53	34.696,00	35.398,42	35.134,00	176.992,10	175.670,00	176.992,10	175.670,00	100,75%
M2	227.442,74	169.000,00	0,00	0,00	59.014,39	118.000,00	71.614,28	71.750,00	358.071,41	358.750,00	358.071,41	358.750,00	99,81%
LENS	200.554,67	196.000,00	0,00	0,00	88.918,06	93.200,00	72.368,18	72.300,00	361.840,92	361.500,00	361.840,92	361.500,00	100,09%
CCMIJU	255.451,44	229.400,00	0,00	0,00	117.341,24	122.960,00	93.198,17	88.090,00	465.990,85	440.450,00	465.990,85	440.450,00	105,80%
IC	182.874,71	246.461,00	0,00	0,00	18.043,82	40.133,00	50.229,63	71.648,50	251.148,16	358.242,50	251.148,16	358.242,50	70,11%
BIOEF	138.593,83	132.270,00	0,00	0,00	21.445,16	66.100,00	40.009,75	49.592,50	200.048,74	247.962,50	200.048,74	247.962,50	80,68%
OSAKIDETZA	70.413,12	57.730,00	0,00	0,00	0,00	0,00	17.603,28	14.432,50	88.016,40	72.162,50	88.016,40	72.162,50	121,97%
TOTAL	**2.717.302,50**	**2.302.961,00**	**0,00**	**0,00**	**652.132,29**	**895.163,00**	**842.358,70**	**799.531,00**	**4.211.793,49**	**3.997.655,00**	**4.211.793,49**	**3.997.655,00**	**105,36%**
% Spent		**118%**		**#¡DIV/0!**		**73%**		**105%**		**105%**		**105%**	

Declared [1] effort and costs declared in the project

Foreseen [2] foreseen data for the whole duration of the project

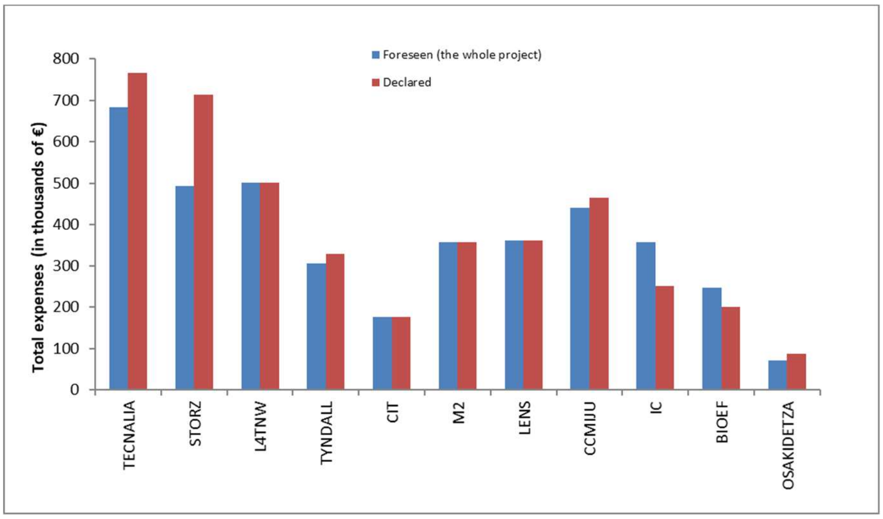

Figure 8 – Partners total expenses, M1-M45

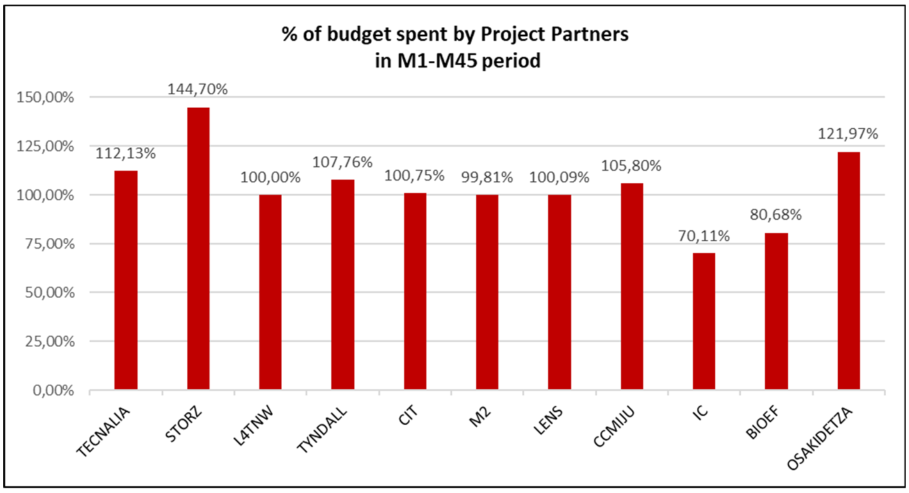

Figure 9 - % of budget spent by partners, M1-M45

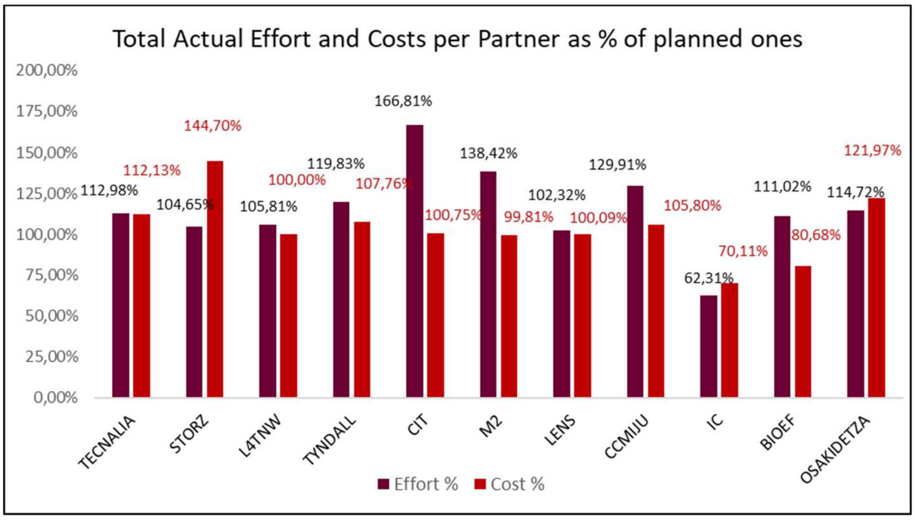

Figure 10 - Total actual effort and costs per partners as % of planned, M1-M45

Disclaimer

This deliverable has been prepared in the context of the funded project PICCOLO. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 732111.