

# A process modelling approach to assess the impact of teledermatology deployment onto the skin tumor care pathway

Tu Anh Duong, Guillaume Lamé, Ouidad Zehou, Charbel Al Skayem, Patricia Monnet, Mohammed El Khemiri, Sonia Boudjemil, Gaëlle Hirsch, Pierre Wolkenstein, Marija Jankovic

# ▶ To cite this version:

Tu Anh Duong, Guillaume Lamé, Ouidad Zehou, Charbel Al Skayem, Patricia Monnet, et al.. A process modelling approach to assess the impact of teledermatology deployment onto the skin tumor care pathway. International Journal of Medical Informatics, 2021, 146, pp.104361. 10.1016/j.ijmedinf.2020.104361. hal-03035103

# HAL Id: hal-03035103 https://hal.science/hal-03035103v1

Submitted on 22 Jan 2021

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers. L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

A process modelling approach to assess the impact of teledermatology deployment onto the skin tumor care pathway

Tu Anh Duong, MD, PhD<sup>1,2</sup>

Guillaume Lamé, PhD<sup>3</sup>

Ouidad Zehou, MD<sup>1</sup>

Charbel Skayem, MD<sup>1,4</sup>

Patricia Monnet<sup>1</sup>

Mohammed El Khemiri<sup>3</sup>

Sonia Boudjemil<sup>3</sup>

Gaëlle Hirsch, MD<sup>1</sup>

Pierre Wolkenstein, MD, PhD<sup>1,5</sup>

Marija Jankovic, PhD<sup>3</sup>

<sup>1</sup> Department of Dermatology, Hôpital Henri Mondor, APHP, Créteil, France

<sup>2</sup> Chaire Avenir Santé numérique, Equipe 8 IMRB U 955, INSERM, Université Paris Est Créteil, Créteil France

<sup>3</sup> Université Paris-Saclay, CentraleSupélec, Laboratoire Génie Industriel, Gif-sur-Yvette, France.

<sup>4</sup> Paris Diderot University, Paris, France

<sup>5</sup> EA- 7379, UPEC, Créteil, France

Correspondance to

Tu Anh Duong, MD, PhD

Department of Dermatology

Hôpital Henri Mondor 51 av du maréchal de Lattre de Tassigny

94000 Créteil, France

Tel /Fax : 00 33 1 49 81 25 12

E-mail : <u>tu-anh.duong@aphp.fr</u>

Abstract word count: 231

Word count: 2248

References: 20

Table: 2

Figure: 1

Abbreviations

Teledermatology TD

Non melanoma skin cancer NMSC

Information and communications technologies ICT

#### Abstract

*Background:* In dermatology, telehealth was raised as a potential answer to increase access and decrease delay for skin cancer management, especially in the elderly population. However, the influence of teledermatology in the care pathway of non-melanoma skin cancer (NMSC) has never been studied.

*Objectives:* To evaluate teledermatology (TD) deployment implications in NMSC care pathways by comparing a conventional care pathway prior to TD integration to the pathway after TD implementation using a process modelling approach.

*Patients and Methods:* Two retrospective studies were conducted in a department of dermatology with an ongoing TD program with geriatric institutions. One study (study 1) mapped NMSC care pathway prior to TD integration from January to February 2013. Another determined NMSC care pathway (study) for patients managed after TD diagnosis from September 2016 to October 2018, during the same period patients managed by conventional care process were used as controls. Patients characteristics, type of tumors and processes were compared using time as a key performance indicator.

*Results:* 89 NMSC patients were managed in the department (mean age= 76 yr old  $\pm$  13) during the study 1 period while from September 2016 till October 2018, 36 patients NMSC were managed after TD, mean age of 89 years old  $\pm$  6 and 681 patients were managed in a conventional process, mean age of 78 years old  $\pm$ 12. There was no significant difference in delays between: first in-person or TD consultation and biopsy, biopsy and multidisciplinary consultation, or biopsy and surgery. NMSC patients consulting through TD had significantly longer delays between: first consultation and multidisciplinary consultation, multidisciplinary consultation and surgery, and first consultation and surgery (p=0.037, p=0.02, p<0.005, respectively).

*Conclusion:* Interestingly, patients managed by TD were significantly older than those managed using a conventional care pathway, confirming TD interest to improve access to care for underserved populations. Unexpectedly their total time spent in the process was not shorter. The results of this analysis illustrated the interest of using process modelling approach to assess the impact of a healthcare innovation integration and to further rethink coordination and care pathways for NSMC post TD.

**Key words:** teledermatology, evaluation, non-melanoma skin cancer, care pathway, access to care , process modelling, telehealth, telemedicine

## Introduction

Teledermatology (TD) is a care delivery innovation enabling remote diagnosis and management. This new modality for healthcare delivery uses information and communications technologies (ICT) to send clinical images or data for a remote medical expertise. It is considered as a promising leverage to improve care access for underserved populations. Pilot studies have lately established its reliability in comparison to face-to-face dermatology visits and suggest that it could be an alternative for in-person pigmented lesion clinic visits.<sup>1–3</sup> Cost benefit studies have tried to demonstrate the economic benefit of implementing this innovation.<sup>4</sup> Based on these encouraging results, we believe that TD implementation could be an essential asset for healthcare systems, in order to provide better care and management, even if structured pathways after a TD consultation are yet to be established.

For many experts, TD is considered as an efficient tool if it avoids up to 30% of in-person referrals and unnecessary travel, or if it increases primary care physicians' knowledge and skills in dermatological disorders.<sup>5–7</sup> In this context, skin cancer is a good option for teledermatology deployment. The incidence of skin cancer increases with age, and its management mainly relies on early and appropriate surgical removal of the tumor to decrease morbidity. According to guidelines, a biopsy prior to any surgery is needed to define the tumor type and the additional margins if necessary.

Considering TD as a healthcare delivery innovation, we used a process modelling approach,<sup>8</sup> in order to compare the pathways followed by patients consulting through TD and through regular in-person consultations. The aim of this study is to compare conventional care process and TD care process in the management of non-melanoma skin cancer (NMSC).

#### Methods and materials

#### **Study setting**

This study was conducted in the dermatology department of Henri-Mondor University Hospital. This department developed and implemented in routine practice a secured store-andforward TD process using a regional secured platform in 2016, connecting geriatric institutions to a department of dermatology. Requesting physicians used a standardized form

to request dermatological advice. Our objective is to compare the pathway followed by NMSC patients who first consulted in the conventional way (in-person) and those who first consulted through TD at 2 geriatric institutions. Two retrospective studies were those conducted:

<u>Study 1:</u> The conventional care process (prior to TD implementation) was mapped using a standard engineering process modelling approach. To model the conventional care process, we interviewed experts (n=5) to identify the activities and processes needed for skin tumor management. A generic process was designed then applied to all the patients managed for a skin tumor in the department. Based on this process model, pathway data were collected for each patient seen in January and February 2013.

<u>Study 2:</u> Care pathway data for the TD care process and the conventional care process were collected retrospectively for each patient who attended the same hospital for NMSC management between September 2016 and October 2018.

# **Participants**

All participants were adults  $\geq$  18 years old with a histological confirmed non-melanoma skin cancer. All participants were managed in the department.

<u>Study 1:</u> Patients included were adults with NMSC managed in the department of dermatology in January and February 2013. For each patient, the care process was determined, from the first consultation in the department until the last step of the cancer treatment (margin surgery or other therapeutic managements, e.g. radiotherapy).

<u>Study 2</u>: Patients included were adults with confirmed NMSC diagnosed via TD from September 2016 to October 2018. For all patients, all the steps from the first TD consultation through TD until the last step of the tumor treatment were retrospectively collected. For non-TD, in-person NMSC pathways, the delay between multidisciplinary consultation and surgery was collected.

# **Collected data**

For both studies, data were collected from patients' electronic records and the appointment booking software of the hospital, or from the TD platform. Relevant process activities were determined with experts. We retrospectively identified the following steps: dermatologist's

consultation, skin biopsy, multidisciplinary consultation, and surgery. Data were collected for consultation dates, and for the TD group, for the number of missed appointments. Cancer type, e.g. basal cell carcinoma (BCC) or cutaneous squamous cell carcinoma (SCC), was recorded. All patients declared non-opposition to anonymous use of their data, the database was declared to the "Commission Nationale Information et Libertés".

#### Statistical analysis

The conventional and the TD care pathways were compared using time indicators (days): time between the first consultation and the biopsy, time between the first consultation and the multidisciplinary consultation, time between the first consultation and the surgery, time between the multidisciplinary consultation and the surgery. Population characteristics were compared. Moreover, we also compared age, skin cancer distribution and delay from the multidisciplinary consultation till the surgery, between the TD group and the conventional group during the same period of study 2 (2016-2018). We also compared the characteristics of NMSC patients who received conventional care (non-TD) in 2016-2018 and in 2013.

Data were analyzed using SPPS<sup>®</sup> statistics software. Qualitative variables are expressed as percentages and quantitative variables as mean or median (range). Categorical variables are compared using the Chi-square test, continuous variables using the t-test or the Kruskall Wallis test. All tests were 2-tailed.  $P \le .05$  indicated statistical significance. This study was approved by the institutional review board of CPP Ile-de-France II.

#### Results

#### Patients

Study 1: In January and February 2013, 89 NMSC patients were managed in the department (mean age= 76 yr old  $\pm$  13).

Study 2: From September 2016 till October 2018, 36 patients NMSC patients consulted via TD and were later managed in the department, with a mean age of 89 years old  $\pm$  6. During this same period, 681 patients with NMSC consulted "in-person" and were later managed in the department, with a mean age of 78 years old  $\pm$ 12.

#### Care pathway modeling

Four types of activities were identified; their sequence order in the process may have varied from a patient to another. Figure 1 summarizes both the conventional care process within the hospital and the care process with and after TD consultation. The main difference is in the patient's enrollment in the hospital care process. In the conventional care process, biopsy is always the first step, followed by three options: surgery, multidisciplinary consultation or second dermatology consultation, before surgery scheduling. In the TD care pathway, some patients skipped the biopsy as they were directly scheduled for a surgery.

## **TD** process care pathway

The TD skin cancer care pathway was established for 36 patients. All had a skin biopsy, and 28 had a scheduled surgery (78%). Most of the patients (n=22; 61%) benefited from the dermatological diagnosis the same day the TD consultation was sent. The median time between expertise consultation and biopsy was 16 days [2-126], and the median number of steps before treatment was 3 [1-5]. Thirteen patients (36%) had one missed biopsy or surgery visit. Biopsy was most frequently the first step in the hospital after TD (n=32, 89%), while three patients had a direct surgery. More than half of the patients (n=18) completed their process in 3 steps to surgery.

#### **Population comparison**

Table 1 compares the characteristics of the two populations. Patients in the TD group were significantly older, and more likely females. SCC was more frequently observed in the TD group than in the conventional care group. The number of scheduled surgeries did not significantly differ between the two groups.

In comparison to patients enrolled in the conventional care pathway in the same period 2016-2018, patients in the TD group were significantly older 89 years old  $\pm$  6 vs 78 years old  $\pm$ 12, p <10<sup>-3</sup> with the same cancer type distribution.

For patient enrolled in the conventional care process, the comparison of patient characteristics between 2013 (n=89) and 2016-2018 (n=954) did not display any significant differences in age, p=0.2, or the presence of a scheduled surgery [76% (n=68) in study 1 vs 82% (n=556) in study 2, p=0.25]. NMSC distribution significantly differed between the two groups with more SCC in 2013 [51% (n=49) vs 43% (n=296)] and fewer BCC [40% (n=35) in 2013 vs 54% (n=367) in 2016-2018], with p <10<sup>-3</sup> for both.

#### Care pathway (process) comparison

Care pathway (process) comparison between study 1 and 2 did not highlight any significant difference in delays between: first in-person or TD consultation and biopsy, biopsy and multidisciplinary consultation, or biopsy and surgery. NMSC patients consulting through TD had significantly longer delays between: first consultation and multidisciplinary consultation, multidisciplinary consultation and surgery, and first consultation and surgery (p=0.037, p=0.02, p<0.005, respectively) (Table 2).

For the conventional care group, in comparison to 2013, the mean time between the multidisciplinary consultation and the surgery was significantly longer in 2016-2018 (28 days  $\pm 21$  in 2013 vs 37 days  $\pm 21$  in 2016-2018, p <10<sup>-3</sup>). Finally, compared to the conventional group during the same period, the TD group had a longer delay between multidisciplinary consultation and surgery 46 days  $\pm 30$  vs 37 days  $\pm 21$ , p=0.068)

#### Discussion

Studies comparing telemedicine or teledermatology to conventional care have mostly focused on diagnosis outcome comparing standard care to telemedicine, using methodologies such as before-and-after studies, randomized controlled trials or cost-benefit studies.<sup>4,9,10</sup> Process modelling is a relevant approach to assess the impact of an innovation integration on a conventional process. It enables the identification of new resources or activities, using process comparisons through key performance indicators such as time, cost or resources. It was successfully used to represent or assess areas of improvement in healthcare systems.<sup>11,12</sup> In the field of skin cancer management, studies including TD mostly focused on the accuracy of this platform in the diagnosis, there are few data on the pathway of skin cancer patients after TD consultation.<sup>13</sup> Herein considering teledermatology as a care delivery innovation we used a process modelling approach to retrospectively compare TD to conventional care for NMSC, describing processes using key performance indicator while describing the concerned population.

In our study, patients in the TD group were significantly older than those in the conventional group. This is because most TD patients are in residential institutions like nursing homes, so their primary physicians resort to TD to avoid unnecessary travels.<sup>14,15</sup> Since they are older, this explains why SCC was more common in the TD group. In the conventional group, there was less SCC in 2016-2018 compared to 2013. In comparison, other studies showed that

between 2013 and 2015, the incidence of SCC was plateauing or falling in Australia, and it was stable in the United States (2013–2015).<sup>7</sup>

Compared to the conventional group in 2013, the TD group in 2016-2018 had a longer time between the first consultation and the multidisciplinary consultation, the multidisciplinary consultation and the surgery, and the first consultation and the surgery, which can be seen as counterintuitive. This can be explained by the fact that TD patients are older, and shorter delays are usually given for younger patients with more serious conditions like melanoma. TD patients are also prone to have comorbidities, which would require preoperative screening before anesthesia and surgery, also explaining a longer time to surgery. They also had longer time between the first consultation and the multidisciplinary consultation, compared to the conventional group in 2016-2018. Moreover, in the conventional group, the mean time between the multidisciplinary consultation and the surgery was significantly longer in 2016-2018 compared to 2013, either because of a higher number of SCC which require a prompt management in comparison to BCC or because of an increase in the number of skin cancer patients throughout the years.<sup>6</sup>

Unexpectedly, the overall care process of NMSC through TD is longer than the conventional pathway. Though TD remains a platform for patient triage in dermatology,<sup>16,17</sup> and though access to care is faster through TD, our study shows that after care access, the overall duration of the care pathway is not shorter through TD. TD patients consulting for suspicious malignant lesions are usually old with poor health. They might not be considered as a priority for giving them short delay appointments. Moreover, they sometimes are in palliative care with poor prognosis. We assume that this is why some appointments in the TD group were missed. However, further studies are needed to identify the profile and general conditions of patients with an incomplete pathway. In poor patient conditions where NMSC surgery is unnecessary, dermatologists have to discuss their cases with general physicians. Finally, a way to decrease the lead time to surgery in TD patients is for general physicians to perform skin biopsies, then patients could directly come with their histology result. Though the accuracy of biopsies by non-dermatologists is lower than that by dermatologists, TD can be a platform to guide GPs about the site and method of biopsy.<sup>18</sup> Our results support that TD may facilitate skin conditions management in underserved populations.<sup>19,14,20</sup> Those patients may not have benefited from a dermatological diagnosis without TD. Implementing TD for skin cancer remains a priority given the suitability of this skin condition to remote diagnosis.

#### Conclusion

Access to care for a suspicious NMSC might be accelerated through TD. It is also more practical for elderly patients, and a preventer of unnecessary travel. However, the process for NMSC management once the patient enters the care process is not shorter for TD patients, which might be explained by the characteristics of the population enrolled in TD. More innovative strategies are needed to structure the pathway of patients after a TD consultation. Getting familiar with engineering approaches such as process modelling could help physicians to identify and visualize new processes and consequences generated by an innovation integration in an existing healthcare system.

**Author (s) Contributions:** Dr(s) TAD, SB, MEK, PM, OZ, GL and MJ had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: TAD, MJ. Acquisition of data: TAD, SB, MEK, PM. Analysis and interpretation of data: TAD, MEK, OZ, GL, MJ. Drafting of the manuscript: TAD, MJ, CS. Critical revision of the manuscript for important intellectual content: all authors. Statistical analysis: TAD, MEK, MJ. Obtained funding: none. Administrative, technical, or material support: TAD. Study supervision: TAD. All the authors reviewed and approved the final version submitted for publication.

**Conflict of Interest:** Dr Tu Anh Duong received a grant from Basilea Pharm for a first year of PhD.

## Funding sources: None

Acknowledgement: Drs Alexandre Ostojic, Marie-Sophie Gautier, Paul Lestang, Jean-Luc Plaquet. GCS SESAN Ortif platform.

#### **Summary Table:**

- Teledermatology has been raised as an answer to increase access to care and decrease lead time to skin tumor management
- No data about care process after skin tumor management using teledermatology
- Process modelling has been used to assess area of improvement in healthcare systems
- Telehealth assessment has barely used process modelling approach
- This study used process modelling to compare skin tumor care pathway prior and with Teledermatology integration and displays that TD management is not always associated to shorter care pathways

#### References

1. Keller JJ, Johnson JP, Latour E. Inpatient teledermatology: Diagnostic and therapeutic concordance among a hospitalist, dermatologist, and teledermatologist using store-and-forward teledermatology. J Am Acad Dermatol. 2020 May;82(5):1262–7.

2. Hunt WTN, Ali L, Marder H, Sansom JE, de Berker D a. R. A service evaluation between 2-week wait (2WW) skin cancer referrals via teledermatology and the standard face-to-face pathway at a teaching hospital. Clin Exp Dermatol. 2019 Nov 6;

3. Vestergaard T, Prasad SC, Schuster A, Laurinaviciene R, Andersen MK, Bygum A. Diagnostic accuracy and interobserver concordance: teledermoscopy of 600 suspicious skin lesions in Southern Denmark. J Eur Acad Dermatol Venereol. 2020 Feb 7;

4. Snoswell CBp, Finnane A, Janda M, Soyer HP, Whitty JA. Cost-effectiveness of Store-and-Forward Teledermatology: A Systematic Review. [Review]. JAMA Dermatology. 2016 Jun;152(6):702–708.

5. van der Heijden JP, de Keizer NF, Bos JD, Spuls PI, Witkamp L. Teledermatology applied following patient selection by general practitioners in daily practice improves efficiency and quality of care at lower cost. British Journal of Dermatology. 2011 Oct 25;165(5):1058–65.

6. Koelink CJL, Jonkman MF, Van Der Meer K, Van Der Heide WK. Examination of skin lesions for cancer: Which clinical decision aids and tools are available in general practice? Eur J Dermatol. 2014 Apr 11;

7. Stang A, Khil L, Kajüter H, Pandeya N, Schmults CD, Ruiz ES, et al. Incidence and mortality for cutaneous squamous cell carcinoma: comparison across three continents. J Eur Acad Dermatol Venereol. 2019 Dec;33 Suppl 8:6–10.

8. Jun GT, Ward J, Morris Z, Clarkson J. Health care process modelling: which method when? International Journal for Quality in Health Care. 2009;21(3):214–224.

9. Chow A, Soon C, Smith HE, Apfelbacher CJ. Outcome Measurements Used in Randomized Controlled Trials of Teledermatology: A Systematic Mapping Review. Acta Derm Venereol. 2019 Dec 1;99(13):1210–7.

10. Wang RH, Barbieri JS, Nguyen HP, Stavert R, Forman HP, Bolognia JL, et al. Clinical effectiveness and cost-effectiveness of teledermatology: Where are we now and what are the barriers to adoption? J Am Acad Dermatol. 2020 Feb 5;

11. Askari M, Westerhof R, Eslami S, Medlock S, de Rooij SE, Abu-Hanna A. A combined disease management and process modeling approach for assessing and improving care processes: A fall management case-study. International Journal of Medical Informatics. 2013 Oct 1;82(10):1022–33.

12. Leo CG, Mincarone P, Bodini A, Sedile R, Guarino R, Tumolo MR, et al. Obstructive sleep apnoea: Improving healthcare services by combining process modelling and population analysis. International Journal of Medical Informatics. 2019 Jul 1;127:43–51.

 Finnane A, Dallest K, Janda M, Soyer HP. Teledermatology for the Diagnosis and Management of Skin Cancer: A Systematic Review. JAMA Dermatol. 2017 01;153(3):319– 27.

14. Nelson CA, Takeshita J, Wanat KA, Bream KDW, Holmes JH, Koenig HC, et al. Impact of store-and-forward (SAF) teledermatology on outpatient dermatologic care: A prospective study in an underserved urban primary care setting. Journal of the American Academy of Dermatology. 2016 Mar;74(3):484–490.e1.

Bianchi MG, Santos A, Cordioli E. Benefits of Teledermatology for Geriatric Patients:
Population-Based Cross-Sectional Study. Journal of Medical Internet Research.
2020;22(4):e16700.

16. Massone C, Maak D, Hofmann-Wellenhof R, Soyer HP, Frühauf J. Teledermatology for skin cancer prevention: an experience on 690 Austrian patients. J Eur Acad Dermatol Venereol. 2013 Dec 24;

17. Finnane A, Siller G, Mujcic R, Soyer HP. The growth of a skin emergency teledermatology service from 2008 to 2014. Australas J Dermatol. 2016 Feb;57(1):14–8.

18. Anderson AM, Matsumoto M, Saul MI, Secrest AM, Ferris LK. Accuracy of Skin Cancer Diagnosis by Physician Assistants Compared With Dermatologists in a Large Health Care System. JAMA Dermatol. 2018 01;154(5):569–73.

19. Uscher-Pines L, Malsberger RM, Burgette L, Mulcahy A, Mehrotra A. Effect of Teledermatology on Access to Dermatology Care Among Medicaid Enrollees. JAMA Dermatology. 2016 Aug;152(8):905–912.

20. Naka F, Lu J, Porto A, Villagra J, Wu ZH, Anderson D. Impact of dermatology eConsults on access to care and skin cancer screening in underserved populations: A model for teledermatology services in community health centers. J Am Acad Dermatol. 2018;78(2):293–302.

# **Figures and tables**

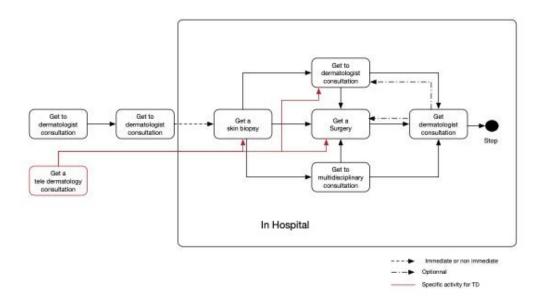


Fig 1: TD and conventional care pathway in hospital process modeling.

	Study 1 Conventional care pathway in 2013	Study 2 TD care process in 2016-18	р
	Number (%) N=89	Number (%) N=36	
Mean age	76 ±14	89 ±6	< 0.005
Female	35 (40)	26 (72)	< 0.005
Basal cell carcinoma	46 (52)	15 (42)	0.19
Squamous cell carcinoma	32 (36)	19 (53)	< 0.005
Basal cell carcinoma plus squamous cell carcinoma	11 (12)	2 (5)	
Scheduled surgery	71 (80)	28 (78)	0.81

Table 1: Population comparison between conventional care process (study 1) and teledermatology (TD) care process group (study 2)

	Mean	Mean		
	Average	Average		
	with	with TD	<b>D</b> 1	
	conventional	care in	P value	
	care in 2013	2016-18		
	(days)	(days) N= 36		
	N= 89		0.00	
Overall time of process	171 ±122	151 ±81	0.98	
Time between the first consultation	17±24	23±24	4 0.008	
and the biopsy	NA= 67	23-24	0.000	
Time between the biopsy and	43±34	81±89	0.3	
multidisciplinary consultation	NA= 51	NA= 14		
Time between the biopsy and the	71 ±43	$59 \pm 84$	0.25	
surgery	N=46	NA=14		
	41 . 20	01.00		
Time between the first consultation	41 ±39	81±88	< 0.005	
and the multidisciplinary consultation	NA=30	NA=14		
Time between the multidisciplinary	25 ±21	46 ±30	0.02	
consultation and the surgery	NA=18	NA=18		
Time between the first consultation	56 ±47	99 ±36	< 0.005	
and the surgery	NA=18	NA=8		
NA – Non available				

NA= Non-available

Table 2: Process time comparison between study 1 and 2