The European InCASA telecare-telehealth electronic platform (PSP-CIP) for the daily assessment of symptoms, weight, and activity in cancer patients on chronotherapy at home

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Background

The circadian timing system drives tolerability and efficacy of cancer chemotherapy

- Self-rated symptoms usually reflect impaired behavioral of biological functions, thus contribute to the Quality of Life (QoL) and impact on prognosis of cancer patients.
- Self-rated symptoms and behavioral functions are controlled by the circadian timing system (CTS),through a network of molecular clocks that time cellular proliferation and drug metabolism (Lévi et al. ARPT 2010) (figure 1).
- Rest-activity monitoring reveals circadian robustness or disruption in cancer patients (figure 2), finding best recapitulated by the dichotomy index I<O, and predicts for Quality of Life and survival (figure 3).

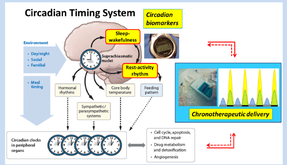

Figure 1: Circadian Timing System. Non invasive monitoring of the rest-activity rhythm provides relevant information regarding the Circadian Timing System which controls cancer treatment mechanisms

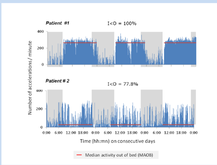

Figure 2: Rest-activity monitoring. Examples of baseline rest-activity records in two patients with metastatic colorectal cancer. Patient #1 displayed a robust circadian pattern, with an I<O of 100%, while patient #2 had circadian disruption, with an I<O of 77.8%. The survival of patient #1 was 37.5 months as compared to 16.6 months for patient #2.

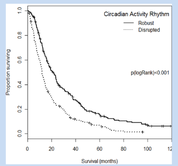

Figure3: I<O prediction of overall survival. Overall survival curves in pooled population of 436 patients with metastatic colorectal cancer according to baseline rest-activity rhythm as estimated with I<O. I<O was determined at time "0" shown on the abscissa. Patients are categorized according to I<O value above or below its median value of 97.5%. Survival curves are compared using Log rank test. Multivariate analyses confirmed I<O an independent prognostic factor.

Circadian chemotherapy (Chronotherapy)

Chronotherapy aims at the reduction of treatment-related symptoms through the adjustment of chemotherapy delivery to the Circadian Timing System. Cancer chronotherapy is delivered at home using programmable pumps, and avoids familial and social disruption. Telemedicine tools can provide continuous information on symptoms, behavior, Quality of Life and Circadian Timing System from non hospitalized patients.

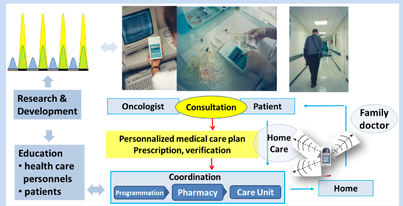

Figure 4: Concept, technology and logistics underlying cancer chronotherapy at home

The inCASA project

- The inCASA project aims at the development of citizen-centric technologies and a service network for chronic disease patients in order both to improve the control of their health condition in their daily life and to minimize hospitalizations.
- This 30-months project is funded by the European Commission. It involves 12 partners in 8 countries.
- There are 5 pilot sites planning a cohort of 130 patients with cancer, neurodegeneration, metabolic syndrome or on a rehabilitation or social program.
- inCASA services will provide continuous information on symptoms, behavior, Quality of Life and Circadian Timing System from patients receiving chronotherapy at home.

Trial design

Objectives:

- To provide daily information on symptoms, quality of life, body weight and rest-activity pattern in 30 patients reveiving chronotherapy at home
- To provide preliminary assessment regarding:
  - the impact on patients quality of life through assessment with SF-36 quality of life scale,
  - the early detection of alteration in health condition through the daily monitoring of symptoms, body weight and rest-activity circadian rhythm,
  - the impact on healthcare management involving physicians, nurses and biomedical technicians,
  - hospitalizations for adverse events

The inCASA platform enables telemonitoring of multiple functions in order to help physicians detect early warning signals in patient condition at home, and prompt adequate and timely intervention. Our pilot site investigates the clinical relevance of daily teletransmitted self assessed symptoms, body weight and rest-activity circadian rhythm in cancer patients.

Endpoints measured through inCASA platform:

- Daily Body weight measurement using Bluetooth weight scale (figure 6)
- Daily Symptoms assessment using M.D. Anderson Symptom Inventory questionnaire on touch screen (figure 7)
- Continuous Rest-activity rhythm recording using an infrared wrist-watch accelerometer (Actigraph). Data are downloaded manually to the platform by the patient once a day (figure 8).

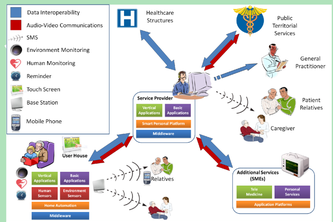

Figure 5: inCASA solution

Figure 6: Body weight. Patients are asked to weigh themselves every day in the early morning using the provided Bluetooth weight scale which communicates with the electronic platform (home Gateway). Data are sent through the GPRS or IP network to a remote service provider.

Figure 7: Symptoms. Daily self-assessment of symptoms by the patient at home in the late afternoon using the MD. Anderson Symptom Inventory scale on the electronic platform. The M. D. Anderson Symptom Inventory is a multisymptom patient-reported outcome measure. It includes 13 core symptom items with highest frequency and/or severity in patients with various cancers and treatment types and 6 items for interference with daily life. It is translated in many languages and widely used worldwide. Symptom items: pain, fatigue, nausea, disturbed sleep, distress, shortness of breath, problem with remembering things, anorexia, drowsiness, dry mouth, sadness, vomiting, numbness. Items for interference with life: general activity, mood, work, relations with other people,

Figure 8: Actigraph and infrared dongle. This Actigraph, developed by Ambulatory Monitoring Inc. (Ardsley, NY, US), is a new version which includes infrared communication for data transmission. Patients are asked to wear the device as a watch day and night and to download the data to the electronic platform once a day using the infrared dongle. The sensor measures the number of accelerations per minute in order to assess the rest-activity rhythm. The downloaded files are sent to a server to be analyzed by the pilot team.

Enrollment

Main inclusion criteria

- Patient suffering from cancer
- Patient living at home
- Ambulatory care
- Written informed consent

Patients are recruited at the Paul Brousse Hospital of Villejuif in France

Pre-Pilot phase

- From November 2011 to February 2012
- Tests of the system in the hospital by 14 patients (9 male, 5 female, 43-77 years)
- 5 patients (4 male, 1 female, 61±13 years) recruited for home monitoring of body weight and symptoms

Pilot phase (ongoing)

- From March to December 2012
- Recruitment of 30 patients for home monitoring of body weight, symptoms and restactivity for a study period of 6+ weeks for each patient
- 10 equipments available

Phase	Period	Patients
Preliminary tests	November 2011	14 patients (9 male, 5 female, 43-77 years)
Pre-Pilot	Nov. 2011 – Feb. 2012	5 patients (4 male, 1 female, 48-64 years)
Pilot	March –December 2012	30 patients

Monitoring & Follow-up

Web portal visualized by clinicians

Changes in body weight, symptoms or activity before, during and after treatment are visualized by the nursing staff through a web portal (figure 9 & 10). If a degradation of the health condition is detected, a nurse calls the patient and alerts if necessary the healthcare professional.

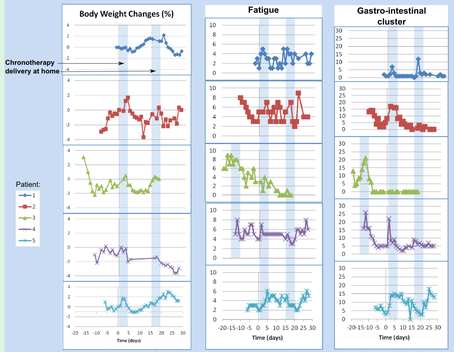

Figure 9: Example of data collected in 5 patients at home during the pre-pilot phase. Five clusters of symtoms have been defined from the core symtoms of the M.D. Anderson Symptom Inventory:
- Gastro-intestinal: nausea + vomiting + anorexia
- Pain and neurosensory: pain + numbness
- Rest-activity: fatigue + disturbed sleep + drowsiness
- Emotion: distress + sadness
- Others: shortness of breath + dry mouth + memory

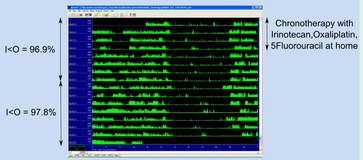

Figure 10: Visualization of the rest-activity rhythm data transmitted to the server by the infrared Actigraph. The rest-activity rhythm is analyzed with the manufacturer software. The computed parameter I<O represents the amount of median activity out of bed compared to the activity in bed. The rhythm is considered as altered (circadian disruption) if I<O is lower than 97.5% (Innominato and al. Int J Cancer 2012 ; Lévi and al. submitted).

Evaluation

- Demographic and clinical dataset
- Quality of life: SF-36 questionnaire administered at the begining, the middle and the end of the study
- Patient perception: NHS WSD questionnaire
- Healthcare professionals perception

Conclusion

The assessment criteria set forth for the inCASA solution will address the issues of:
- patient autonomy,
- Circadian Timing System entrainment in the patient usual environment,
- safety of chronotherapy delivery at home and
- treatment costs.

Its use should induce important organisational changes and perception in healthcare professionals and patients.

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