Development of a Hyperthermic Intra-Peritoneal Chemotherapy Equipment Architecture Based on the Cyber-Physical System Paradigm

Nicoleta Stroia[1], Daniel Moga[1], Corneliu Lungoci[2], Rozica Moga[1], Dorin Petreus[1]

[1]Technical University of Cluj-Napoca, Romania
[2]"Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca, Romania

Abstract. The Cyber-Physical Medical Systems (CPMS) have emerged as an alternative to today's medical device architectures, allowing the development of high-confidence medical equipment. The architecture of a high performance equipment for hyperthermic intra-peritoneal chemotherapy (HIPEC) is proposed, having the structure of the cyber part based on a hierarchical embedded structure suitable for model based development and verification.

Keywords: Cyber-Physical Medical System; Embedded Platforms; Hyperthermic Intra-Peritoneal Chemotherapy.

1 Introduction

In the past decade, the cyber physical system (CPS) has emerged as a paradigm that provides the conceptual basis for architectural frameworks in many complex problems, like health-care, navigation and rescue, intelligent transportation systems[1].

The Cyber-Physical System (CPS) paradigm permits to consider in a unitary way the complex aggregate of patient physiology (including functions and pathologies of diverse organs and systems), the medical devices for diagnosis and therapeutic interventions affecting these systems, and the architecture and overall control of the sensing and treatment system. The Cyber-Physical Medical Systems (CPMS) have specific features like non linearity, transport delays, spatio-temporal effects, and nontrivial aggregation of interactions, particularly due to the close interaction with the human body [2], making their modeling and analysis a difficult task.

High performance equipment for hyperthermic intra-peritoneal chemotherapy (HIPEC) and clinical decision support systems (CDSS) can help implementing in a precise manner the concepts of cytoreductive surgery and regional chemotherapy: the intensification of the cytostatic drugs effect, through the association of hyperthermia.

This would make HIPEC a technique that allows approaching in a therapeutic manner pathologies for which systemic chemotherapy is not an efficient solution, like peritoneal carcinomatosis (PC).

HIPEC requires intra-peritoneal spread of cytostatic drugs, at high temperatures (41-43 C), accomplished within 60-120 minutes, during surgical interventions. In comparison, the central temperature of the body is 37-38 C. HIPEC is superior to the intra-peritoneal administration of cytostatic drugs, because the association of hyperthermia has a series of advantages: cytotoxic effect directly on the malignant cells (even more as the tumor vascularization is better), favors the penetration of cytostatic drugs in tumors, the increase of cytotoxicity of certain chemotherapy substances (most important), by acting at DNA level [3].

The currently accepted (closed procedure) requires the usage of an equipment that can assist in maintaining the intra-peritoneal temperature of the cytostatic fluid in the range 42-43C, as well as in producing an even distribution of the cytostatic fluid flow. The success of this therapeutic technique depends on a deeper understanding of the complex thermal phenomena associated with intra-peritoneal chemohyperthermia and on the availability of innovative HIPEC equipment that exploits this understanding.

The architectural design and the implementation on embedded platform of a HIPEC equipment as a CPMS with high-confidence of its functional correctness is a co-design problem: the design of the cyber part (embedded control systems and networks) and the physical part influence each other.

2 Architectures for Medical Platforms

A CPMS is presented in [2] as a collection of computing nodes distributed in a physical environment. The computing nodes are networked and interact with the physical environment. The cyber-physical interactions (see Fig. 1), can occur between computing entities and spatial regions or particular locations in the environment.

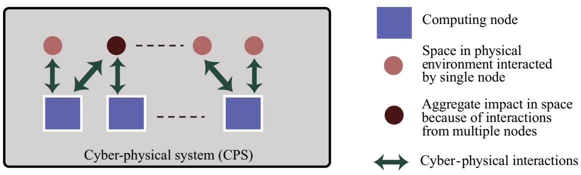

Fig. 1. Cyber-physical system architecture [2]

The report „High-Confidence Medical Devices: Cyber-Physical Systems for 21st Century Health Care” [4], examines the architectures, the development methods and the associated research challenges of the current medical device systems, and clearly identifies the future medical devices as High Confidence Cyber-Physical Systems.

The following ideas are listed among its key findings:

- Today’s medical device architectures are typically proprietary, not interoperable, and rely on professionals to provide inputs and assess outputs.
- When a patient is connected to multiple devices at once, such as in an operating room, clinicians now must monitor all devices independently, synthesize data, and act on their observations.
- While medical device architecture is beginning to include wired and wireless interfaces to facilitate networked communication of patient data, ad hoc efforts to ag-

gregate data across devices designed to operate separately can lead to unintended or accidental results.

- Capabilities as home health care services, delivery of expert medical practice remotely (telemedicine), and online clinical lab analysis underscores the central role of advanced networking and distributed communication of medical information in the health systems.
- Neither past nor current development methods are adequate for the high-confidence design and manufacture of highly complex, interoperable medical device software and systems.
- Today's verification and validation efforts are driven by system-life-cycle development activities that might be inadequate in the context of an increasing components and interactions complexities of the emerging medical devices and systems.

3 Specific challenges associated with HIPEC equipment

First of all, it should be observed that although the cytostatic effect is proportional to the increase of the temperature, the human body is the one that sets the limits: as temperatures exceeding 45-46 C may induce local abdominal injuries and systemic hyperthermia. The main drawbacks of the current equipment are uneven/uncontrolled distribution of the temperature in the target volume and uneven flow distribution (some peritoneal surfaces can be underexposed/overexposed to chemotherapy due to preferential circuits between the inflow and outflow catheter).
These problems are related to the following architectural/operational aspects of the currently available HIPEC equipment:

- there is no appropriate distributed temperature monitoring for providing comprehensive information regarding the intra-peritoneal temperature distribution (the limited, low number of thermal sensors, randomly placed, does not allow the thermal characterization of the entire peritoneal space);
- the uncontrolled flow distribution favored the existence of multiple areas with a temperature that is lower than the appropriate one, compromising the synergic effect cytostatic drug;
- the volumes of the peritoneal cavity are not quantified before starting the HIPEC procedure in order to identify optimal cytostatic liquid volume;
- there are no advanced control mechanisms implemented in order to achieve homogenous temperature in the peritoneal cavity.

A fully automated HIPEC equipment allowing a homogeneous distribution of chemotherapy drugs and heat, able to provide optimal exposure of the patient with minimal exposure of the personnel must reside on an architecture proposed that addresses the following problems:

- complex inflow distribution system with multiple nozzles with variable flow;
- a multipoint temperature measurement system;
- smart control algorithms for localized flow and temperature control;

- hermetically sealed implementation of the devices that have to be sterilized.

The need for “Human Centric Cyber-Physical Systems” emphasized in [5] is more than relevant for the case of CPMS, since here humans will interact with the system directly, leading to the consideration of two basic issues: high-confidence operation of HIPEC CPS and patient safety.

A crucial condition for developing a high-confidence of HIPEC CPS is high model fidelity (i.e. the model accurately imitates the real system). If this condition is met, there is possible to automatically synthesize the model’s cyber parts using Model-Based Design methods, such that the simulated model and the behavior of the real running system coincide.

Patient safety is a primary factor in configuring the architecture of medical devices, and was addressed by a series of standards related to medical equipment design and manufacturing. The IEC 60601 standard has a long history with the original IEC 60601-1published in 1977.According to the 3rd edition (IEC 60601-1, published by the IEC in 2005 and known in Europe as EN60601-1:2006) medical devices will need to pass static testing, dynamic testing, and formal testing (to prove that requirements are met, that the system will be stable, and that algorithms are correctly implemented). The standard defines safety as the avoidance of unacceptable risks of hazards to the physical environment (i.e. to the patient) due to the operation of a medical device under normal or single fault condition. The concept is extended in [2], were the safety of a CPMS is defined as avoidance of risks of the computing unit or the physical environment from harmful effects of cyber-physical interactions.

4 The proposed architecture

The following issues have to be addressed when designing the cyber part of the HIPEC CPS:

- identify those robust embedded platforms that support capabilities such as extended built-in self-testing on the hardware platform, system-level device health monitoring, fault isolation and recovery, hardware-level security implementation, and device attestation;
- align with non-proprietary interoperability standards and provide advanced capabilities for managing the safety, security, and privacy aspects;
- specify latency and real-time, fault-tolerance, and device registration and configurability requirements.

As indicated in [6], various agencies and standards bodies, have signaled that the future of medical technology lies in medical device interoperability, emphasizing the capability to integrate information from multiple clinical sources in a context-sensitive way. Such considerations were the basis for the design of an integrated HIPEC System (see Fig. 2), able to communicate via its Network Interface with a Database Server and a clinical decision support system software (PC DSS) running on a personal computer, and a set of cameras connected through a wireless access point.

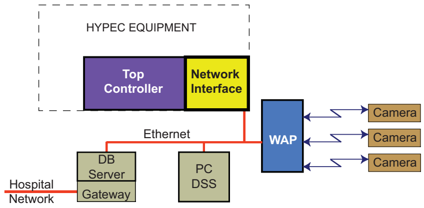

Fig. 2. The integrated HIPEC System

The essential blocks of the proposed HIPEC equipment architecture are indicated in Fig. 3. A dedicated safety controller was included, having its own pressure and temperature sensors and a direct connection to the user interface for immediate error/alarm reporting to the medical staff, as shown in Fig. 4.

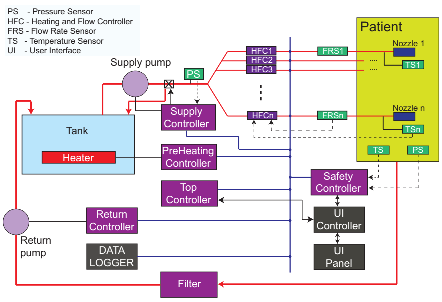

Fig. 3. The essential blocks of the proposed HIPEC equipment architecture

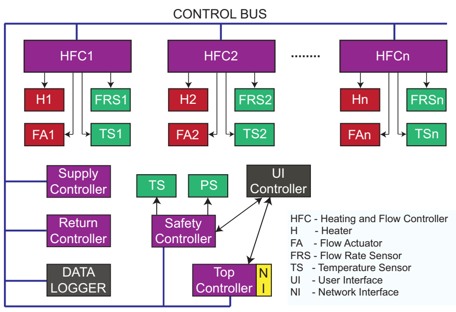

Fig. 4. Cyber part of HIPEC equipment as Cyber-Physical System

The appropriate references can be prescribed to the top controller via the user interface module or through the network interface. The problem of distributed monitoring and control for flow and temperature was addressed by introducing a family of heat and flow controllers (see Fig. 4), all connected to a common bus and having defined a hierarchy with the top controller at the superior level. This approach can accommodate for model based development and testing of heat and flow controllers as identical units, each of them implemented on an individual embedded processor. Since the local temperature sensor and the individual heater for a given flow channel are directly connected to such a controller, the physical properties (like temperature transducer inertia, heating actuator inertia, etc.) would have to be addressed by the software implemented at this level.

5 Conclusions

An innovative approach to the design of a high performance HIPEC equipment was demonstrated through the setup of an architecture in line with several criteria: use of embedded platforms for the cyber part the equipment, compliance with the recommendations for Cyber-Physical Medical System, adequacy to an model based development that can provide a high level of confidence. Future efforts will be made in order to bring the details of the hardware specification to a level appropriate for implementation on ARM platforms as well us for the specification of the software functionality.

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