OPTIMIZED PLANNING OF RADIOPHARMACEUTICAL PRODUCTION IN HOLONIC CONTROL FRAMEWORK

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The short half-lives of radionuclides used in types of radiopharmaceutical products needed for diagnostic imaging or treatment demand a rigorous production planning, in order to assure that high-quality products reach the patients in the required time and the production's radioactive waste is minimized. The paper presents an optimal radiopharmaceuticals production planning system using Constraint Programming (CP). To achieve requirements such as shortest possible production time in safety conditions for the production process, a dual layer control system is proposed: (i) centralized production planning (System Scheduler) and (ii) decentralized SCADA system with distributed intelligence for environment monitoring and control of product making, both layers being integrated in a Holonic Manufacturing Execution architecture (HMES) with multi-agent implementing. Experimental tests were performed on a 19 MeV cyclotron, studying the required products activity dependence on the beam current and irradiation time. These experimental results were then used for the configuration of production timing constraints of the CP-based ILOG OPL scheduling method and optimization engine.

Keywords: Constraint Programming, Optimal production planning, Holonic Manufacturing Execution System, Multi-agent framework

1. Introduction

Radiopharmaceuticals are recognized means for key investigation in many life sciences disciplines, and for diagnosis and treatment of many life-threatening diseases. Produced in specialized nuclear facilities with dedicated radiochemistry equipment, these medical products are used for positron emission tomography (PET) and single photon emission computed tomography (SPECT) [1].

The production of radiopharmaceuticals needs performing two processes: (1) obtaining the radionuclides on which the pharmaceutical is based, i.e. the

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radioactive isotopes of elements with atomic numbers less than that of bismuth; (2) preparing and packaging the final, portioned radiopharmaceutical product.

Proton-deficient radionuclides are usually produced in nuclear reactors [2], whereas neutron-deficient radionuclides are more easily produced using a proton accelerator like the medical cyclotron. Optimized planning and safe control with distributed intelligence for radiopharmaceuticals production is proposed below.

The main challenges of a cyclotron-based radiopharmaceutical production line (with facilities, control and monitoring system) are to make nuclear medicine products of quality in the shortest possible time, safely for employees and the surrounding environment. Such a production line is specialized in making daily planned batches of products in small volumes, according to the orders received from hospitals and PET centres. To be cost-efficient, a production facility must prepare and deliver a minimal number of 10 product vials daily.

While having a specific chemical structure, radioactivity and usage, each product follows the same manufacturing path: radio-isotopes are produced in a particle accelerator (cyclotron), then transferred into technology isolators for chemical synthesis followed by portioning (vial dispensing) of the bulk product, quality control of the final product by conformity tests on multiple parameters; in the last stage, valid products are packed and transported to the clients in shielded containers. The stages for the cyclotron-based production of radiopharmaceuticals are presented in Fig. 1, and involve one functional block (filled in with light grey) for each stage; a fifth stage (s5) should be considered for the transport of the final, valid products to the client (e.g., hospital, diagnose or treatment centres).

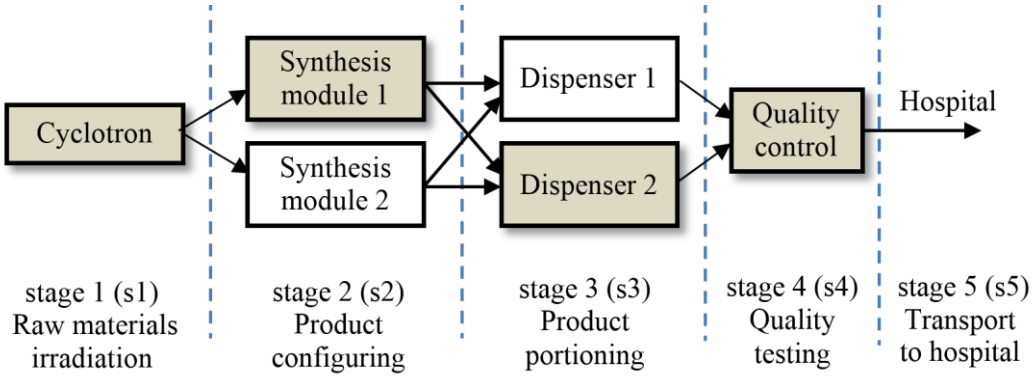

Fig.1. Manufacturing stages for radiopharmaceutical products

Usually, due to its special reliability provided by the manufacturer, and its high acquisition and maintenance costs, production lines of this type have only one cyclotron resource [3] for stage 1 (raw material irradiation). Single points of failure are avoided in stage 2 (product configuring) and stage 3 (portioning of bulk product) by using respectively any of two identical resources (synthesis

modules 1, 2 and robotized dispenser 1, 2) capable to replace each other in the case of breakdown or maintenance works.

The three production resources together with the quality testing equipment are disposed in *flow shop* processing mode: products flow in one single direction [4]. Raw materials enter the cyclotron and are irradiated, the output being fed to one of the synthesis modules where chemical reactions occur; the resulting bulk radiopharmaceutical product is then portioned and eventually diluted in one robotized dispenser hot-cell. Samples of vials are sent to the quality control room in stage 4 for multi-parameter tests; finally, the vials are packed and labelled for transport to the client. The product passes in different stages through capillary tubes from one resource to the next and receives a treatment / operation formalized as service [5].

Due to the specificity of processes transforming and handling radioactive materials and products, the execution of the planned production is conditioned by the continuous monitoring of *safety parameters* (radioactivity, no. of airborne particles) and of *environment parameters* (temperature, pressure and relative humidity) in closed production spaces (clean rooms) and their surroundings [6].

2. The dual-layer control system: HMES and delegate MAS

In order to achieve the requirements above defined (shortest possible production time and safety conditions during production) a control system based on a dual architecture: centralized System Scheduler (SS) for optimal planning at batch product horizon, and decentralized environment parameter monitoring and operations execution with SCADA controlled by delegate MAS (dMAS) – multi-agent system). Both layers: management of product execution and monitoring of facilities' radioprotection and environment parameters are integrated in a holonic execution architecture (HMES), Fig. 2. The global control architecture is multi-layered: a) SS layer - production planning, data base and reports generation; b) application layer with SCADA for operations and ventilation system (HVAC) control; c) resource control layer for parameter monitoring and conditioning. Layers b, c have dMAS.

Production planning is computed off-line and may be reconfigured by the resource monitoring and control layer in case of breakdown or maintenance events. Production execution control is subordinated to HFES – the safety and environment parameter monitoring, conditioning and control system. The control and computing actions of SS and dMAS are exerted in the HMES holarchy as:

Centralized production planning and supervising control: a) long-term strategic resource allocation balancing the usage time of the resources replicated for stages 2 and 3 in the context of scheduled maintenance; b) short-term (24 hours) production planning, optimizing a cost function (minimize: manufacturing

time / raw material waste, etc.); (c) maintaining a production database (product traceability, history of production execution), generating logs and client reports.
Decentralized control of product execution and environment parameters: a) routing and portioning control of the bulk product; b) monitor, condition and control safety and environment parameters in clean rooms at disturbances in order to deliver valid products at agreed deadlines; c) detect resource failures and alarm states of environment parameters to stop production; d) collect and store data at execution time for product traceability and production history.

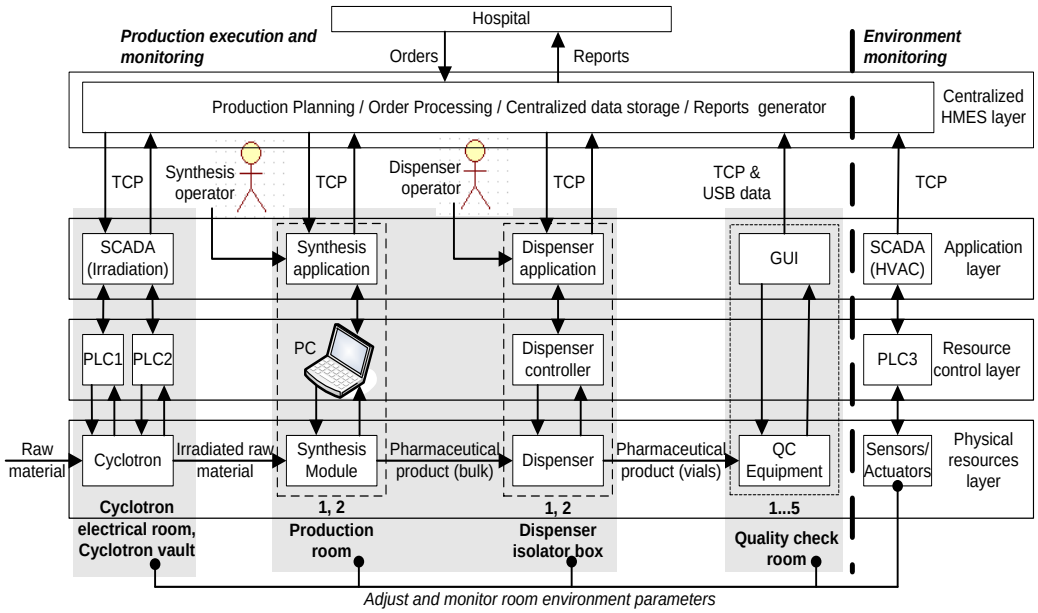

Fig.2.The global control architecture of radiopharmaceuticals production: SS + dMAS = HMES

The control solution is based on PROSA holonic reference architecture [7] and was customized for the flow shop layout and operating mode, in which the product recipe is established during off-line daily production planning from the product data specified by the client (Make To Order production) and embedded in the production orders. The radioprotection safety and working environment parameters strongly affect the production process. This is why the holonic control model is extended with an entity, the aggregate Environment Holon, which computes and integrates on line in a global facility environment model the clean room models, the HVAC parameter conditioning channel models and the HVAC control models and is continuously conditioning the production processes. The multi-agent system showed in Fig. 3 implements the holonic production control.

The control holarchy is composed of the following entities:

The **Supervisor Holon** (SH) is responsible with:

- *Optimizing production*: a) resource allocation subject to a priori scheduled maintenance periods, alternative resource reassigning at breakdown; and b) batch planning and operations scheduling and configuring (e.g. dispensing);
- *Setting orders*: a) transpose hospital order in physical product recipe and execution schedule; b) configure room parameters for planned production;

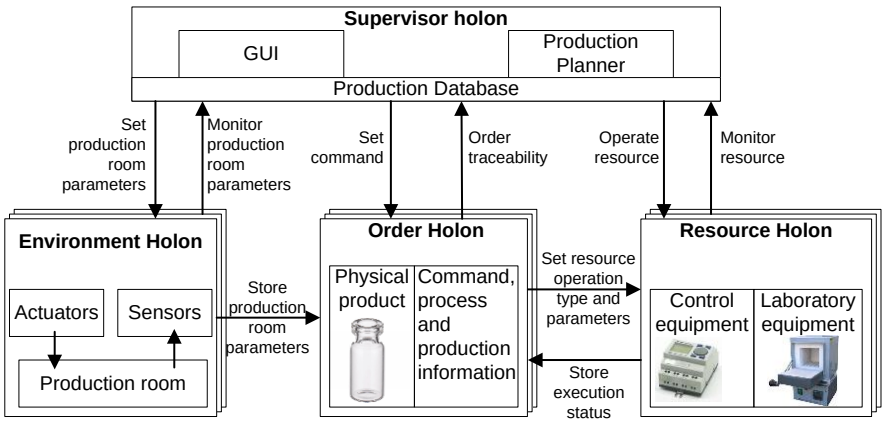

Fig.3. Multi-agent system implementation of the holonic production planning and control (HMES)

- *Authorizing the adjusting of clean room parameters* (e.g., number of particles in the dispenser room) upon request of the Environment Holon;
- *Centralizing data* about resource status, process rooms parameters and product execution; s*toring* production logs / history files in the Production Database;
- *Generating traceability reports* of radiopharmaceuticals produced;
- *Keeping updated* BOM (Bill of Materials).

The **Resource Holons** (RHs) encapsulate both the information/decision part and the associated physical resource used (e.g., cyclotron, synthesis module, dispenser and quality test equipment). Each physical resource is controlled as an independent automation island, and the objective of the control architecture is to integrate in a uniform manner these islands (modelled as RHs) by help of the SH for Order Holon (OH) execution [8].

The **Order Holon** (OH) holds the information needed to fulfil a client order: recipe specification (activity level, irradiation time and current, diluting quantity / vial) derived from the requested product data; production information used for resource and environment parameterization; execution information for each stage. The OH is an aggregate entity consisting of: (1) client identification data (product type, radioactivity level, hospital, and delivery time); process execution data (recipe specifications, resources, operations parameters as resulted from batch planning); traceability data (resource and environment state during product making, values of execution parameters, and (2) the portioned product.

The **Environment Holon** (EH) checks if the process and environment parameters are in normal value ranges, validates the operations executed by RHs and triggers alarms when radioactivity levels exceed normal values or when the evolution of other parameters endangers human safety or alters product quality. EH monitors the *pressure* in the cyclotron vault, production room and dispenser isolator box; the *temperature*: in the cyclotron's electrical room, production room and dispenser isolator box; the *relative humidity* in cyclotron's electrical room, production room and dispenser isolator box; the *number of particles* in the dispenser box (if the number of particles is not in range the control waits for max. 20 minutes - recovery time to allow this parameter to re-enter in range; if it re-enters the range the process resumes, dilution is recalculated and dispensing is delayed with the corresponding amount of time – which also delays delivery; otherwise production is abandoned and the production order fails); *radioactivity* levels in the production room, control room and dispenser room.

The operation of the aggregate EH is controlled by a multi-agent system acting as master over the HMES production management layer, in the sense of conditioning product execution by radioprotection safety and environment status.

3. Optimization of production planning

The production planning process was designed to optimize the execution of radiopharmaceutical products such as to undertake as much demands as possible while minimizing the production time and respecting the constraints imposed by the physical installation, the environment and by the client (hospitals, PET centres).

With the increase of the patients' number, there has been a corresponding increase in the number of patient scans that have been cancelled because of various reasons, as statistics from a Canadian PET imaging centre in [9] shows in Table 1. Problems with ^{18}F-FDG production have been the most frequent reason for cancelled scans in each year of operation, and the number of scans cancelled because of this has doubled practically in each year of operation.

Table 1

PET/CT scan cancellation reasons / year

Year	Scans cancelled because of ^{18}F-FDG production problems	Scans cancelled because of transport problems	Scans cancelled because of PET system downtime
2005-2006	45	32	3
2006-2007	84	28	0
2007-2008	165	57	10

In the production planning development process the following terms have been used: *demand* (one vial needed by a hospital), *command* (a set of demands

that are produced together and contain the same type of product) and *batch* (the set of all demands that must arrive at the same hospital; a batch can contain different products). The final product can be delivered to the hospital as: *single doze* (one vial will be injected in one patient) or *multi doze* (one vial will be portioned at the hospital for multiple patients).

In this context, the planning problem is formalized by:

- An **input set of data** representing the demands which are characterized by (product type, activity level, client, delivery date):
  - {*demands*} = {(product type, activity level, hospital, delivery time, requested volume)$_i$, i = 1…n; n is the total no. of vials requested for the current day}
- The **decision variables** describing:
  - How are allocated the individual demands to commands:

    {*where*} = {(command)$_{index}$, command=1…m, *index* = 1…n; m is the max. number of commands that are processed within a day; n is the total number of vials requested for the current day};
  - How are processed the commands:

    {*commands*} = {(starting time, maximum irradiation, quantity of enriched water, product type)$_j$, j = 1…m; m is the maximum number of commands that are processed within a day };
  - If individual demands are processed:
    {*processed*} = {(true/false)$_{index}$, *index* = 1...n, indicating whether demand *i* is processed or not due to invalid constraints such as tight delivery time}.
- The **constraints**:
  - The sum of all volumes of the demands within a command should be less than the volume of the irradiated target:

$$\sum_{i=1}^{n} V_i * \frac{desired\ activity_i}{\text{maximum activity}} \leq \text{target volume} - \text{loss}$$

    where: demand *i* will be produced within the current command, V_i is the requested volume of demand *i*, "desired activity$_i$" is the activity of the product in demand *i*, "maximum activity" is the activity at which is irradiated the raw material for the current command, "target volume" is the maximum raw material quantity that can be irradiated in a production cycle, and "loss" is the quantity of product that is lost during transport from one stage to another.
  - Each demand should have the required activity at the requested delivery time for all demands within command *k*, $1 \leq k \leq m$:

$$starting\ time\ + \sum_{r=1}^{4} Tr\ + T5(i) < delivery\ time_i, 1 \leq i \leq n$$

where $T1 \ldots T4$ are the maximum delays when executing the current demand (irradiation time, synthesis time, dispensing time, quality testing time) and T5(i) is the maximum transportation time to the related hospital.

- Do not use the production facility over maintenance periods:

$$\text{production intervals} \cap \text{maintenance intervals} = \emptyset,$$

where "production intervals" are defined by the starting time of the command and its duration and "maintenance intervals" are predefined based on a fixed scheme which takes into account the resources' usage.

- Possible **objective functions**:
  - Minimize production time (optimization problem) at command level;
  - Minimize the number of commands for daily client orders;
  - Minimize the quantity of daily lost raw materials.

By analysing the above requirements, it can be seen that the optimization problem is a matching problem (which demand is allocated to which command), subject to a set of constraints (delivery dates of the vials with a given quantity and radioactivity level). Since there is flexibility when irradiating raw materials (less material can be irradiated at a higher level, and then diluted when dispensing), an objective function represented by production time was added. The planning task deals with *combinatorial optimization* and detailed scheduling, both aspects being tackled in literature by Constraint Programming (CP) approaches [10].

The above described approach is used for the radiopharmaceuticals production process both for *optimized offline planning* (minimize production duration while respecting imposed deadlines – **offline run**) and for *online agile execution* (online adaptation to variations of environment parameters which can delay commands being executed within the same day – **online run**):

Off-line run

1. Demands are gathered for the next production day.
2. Maintenance restrictions are introduced as constraints into the CP model.
3. The ILOG – OP model [12] is called based on the set of demands for the next day:
   a) If a feasible solution is reached, the demands are accepted as received and the production plan is transmitted to the distributed operating control level in order to be implemented;
   b) If no feasible solution is reached (due to conflicting time constraints or tight deadlines) new deadlines are proposed based on the maximum load of the production system and on the rule "first came first serve" in order to fulfil as much as possible demands.

On line run

- Apply process and environment parameter configuring via dMAS according to the off line computed commands.
- Measure environment parameters which affect production time (dust particles in dispensing room and radioactivity levels).
- If parameters are out of range and the current command is delayed re plan the next commands taking into account the new constraints. For any command, since the maximum allowed delay in production (30 min) is less than the maximum delay at delivery (1h) the worst-case scenario is to use the off-line computed production plan and just delay it.

ILOG OPL optimization sequence

The following optimization sequence will be run for a maximum amount of raw material max_irr_vol (capacity of max. irradiated target) processed for any command:

1. Consider all demands valid for scheduling (*processed*(*d*) = true, *d* = 1...n);
2. Order demands based on product type;
3. Choose the highest irradiation level required (all other products will be diluted in order to obtain an inferior irradiation level) for each product type (max_irr_level);
4. For all demands with the same product type compute the sum:

$$\text{sum\_prod} = \sum_{for\ all\ products\ of\ same\ type} requested\ volume \cdot \frac{desired\ irrad.level}{\text{max. irrad. level}}$$

Clearly, $\text{sum\_prod} \leq \text{max\_irr\_target}$.

5. Based on the requested product quantity (sum_prod), on the maximum irradiation level (max_irr_level) and on the number of vials, an estimated production time (makespan) for the demands is computed, considering $Ti, 1 \leq i \leq 4$
6. Test if the production intervals with the width computed at step 5 can be scheduled one after another, with a break between them of 1:30 hours (resource checking periods between successive commands execution, see Fig. 2), without invalidating the delivery times for each demand:
   - For all *c* in commands
   - For all *d* in demands
     - *p* = the command processed before (*c)*
     - If *p* = null (*c* is the first command to be produced)
       - YES: production starting time(*c*) = 6:00 (the installation begins to function at 6:00 in the morning);
       - NO: otherwise production starting time(*c*) = production ending time(*p*) + 90 min;
     - If (delivery_time(*d*)) < makespan(*c*) + production break + production starting time(*c*)
       - NO: Eliminate demand d from the schedule (processed(d) = false) and goto 2
7. Compute the remaining raw material quantity (rem_raw_mat) that can be used with the associated deadline and maximum irradiation level
   - For all *c* in commands
   - For all *d* in demands, processed(*d*) == true

  - rem_raw_mat(*c*) = max_irr_volume – sum_prod

8. Test if the demands eliminated can be produced using the remaining raw material quantity computed at step 7
   - For all *c* in commands
   - For all *d* in demands, processed(*d*) == false
     - If the product of demand *d* is the same as the product manufactured in command *c* and there is enough remaining raw material in command *c* to produce demand *d*:
       - Propose a new delivery time for demand *d*;
       - Set processed(*d*) == true
       - Recompute sum_prod for command *c* with the new considered demand *d*
       - Goto 7

The output of the ILOG OPL optimization sequence used in Off-line run step 3 consists of: (1) the demands scheduled for production based on imposed or negotiated delivery times, and (2) the unfeasible demands that cannot be produced due to the too tight deadline. The optimization sequence is run one day before production execution and the processed quantity of raw material is limited to the quantity of the irradiation target. Any command greater than the maximum raw material quantity that can fill the cyclotron's irradiation target is not considered.

4. Experimental results and discussions

The ILOG sequence described in the previous chapter was tested on a set of 20 demands grouped into two different product categories (FDG with product type 1 and NaF with product type 2). The execution times are described in Table 1 for each stage: irradiation, synthesis and dispensing. The characteristics problem along with the demands, which represent the input to the optimization algorithm, are described in Tables 2 and 3 below.

Table 2

Problem characteristics

Production system capability	
the maximum raw material quantity that can be irradiated in the cyclotron	3500µL
the number of product types	2
number of demands	20
maximum number of commands	2
maximum irradiation level	1500MBq
minimum irradiation level	500MBq
number of hospitals	4

Table 3

Hospital demands

Index	Activity (MBq)	Product type	Quantity (µL)	Hospital (ID)	Delivery time (min from 0:00)
1	500	2	500	2	1200
2	600	2	500	2	1200
3	1200	2	500	2	900
4	700	1	500	4	900
5	900	1	500	2	600
6	1300	2	500	3	960
7	800	2	500	2	960
8	1400	1	500	4	1080
9	700	1	500	1	600
10	1300	2	500	4	660
11	1300	1	500	2	720
12	1100	1	500	4	720
13	600	2	500	4	840
14	700	2	500	3	1080
15	1200	2	500	4	840
16	600	2	500	1	1140
17	1400	1	500	3	1020
18	1400	1	500	2	1140
19	1400	1	500	2	840
20	900	1	500	1	660

If produced individually, the starting time of each demand would be computed based on the activity (how much time the raw material stays in the cyclotron) and on the product type (what type of synthesis is applied to the irradiated raw material). To this amount of time a fixed duration must be added for dispensing and a fixed duration for installation cleaning (1:30 hours). The sum between the irradiation time, synthesis time, dispensing and cleaning time is the time needed to execute each demand. The starting time is computed by subtracting the production duration from the delivery time. A theoretical scheduling is given in Fig.4.

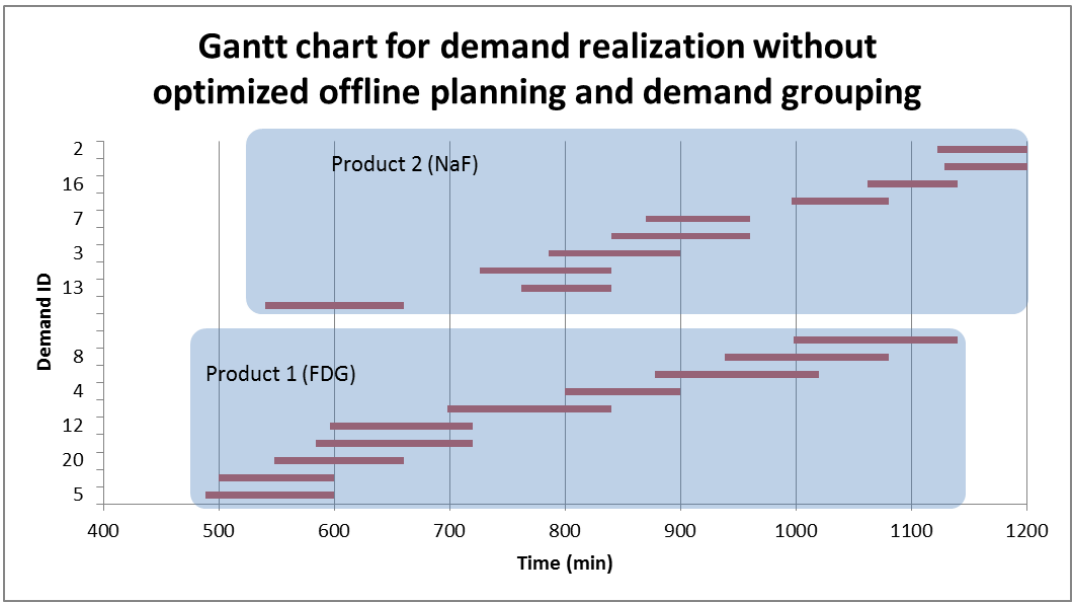

Fig. 4. Gantt chart for demand realization without optimized offline planning

Analysing Fig.4 it can be seen that there are overlapping cases between the production times of the demands which makes it impossible to execute all of them individually even if the cleaning time is not considered as is the case in Fig.4.

If demands are grouped manually in commands, based on production rules, it would also result in an inferior usage of the system and also it would take time to discover the optimum rules to maximize the number of demands. This process is also iterative because after establishing a command and computing its deadline and material usage, the demands chosen initially have to be validated (ex.: demand due date should be greater than command deadline). An example is given in Table 4 where the following production rules have been chosen (i)group demands into commands based on product type, ii) schedule for realization demands from each command until the target is full, iii) compute the command finish time, iv) repeat until all commands are processed and sequence them, v) verify if demand due date is greater than command finish time). The demands with red are rejected either due to the fact that they do not fit in the available production window or because there is no space in the target to irradiate additional material. The formula used for computing the interval in which is executed the command is as follows: T_{start} for the first command is 7:00 (420 minutes from 0:00) and the dimension of the intervals are computed by adding the cyclotron time (0.06*maximum_irradiation_level+30), synthesis time (23 minutes for FDG and 7minutes for NaF) and dispensing time (5 min for the 1st vial, then 2 min for each next vial).

Table 4

Demand allocation based on production rules

Index	Activity (MBq)	Type type	Quantity (µL)	Hospital (ID)	Delivery time (min from 0:00)
5	900	1	500	2	600
9	700	1	500	1	600
20	900	1	500	1	660
11	1300	1	500	2	720
12	1100	1	500	4	720
19	1400	1	500	2	840
4	700	1	500	4	900
17	1400	1	500	3	1020
8	1400	1	500	4	1080
18	1400	1	500	2	1140
10	1300	2	500	4	660
13	600	2	500	4	840
15	1200	2	500	4	840
3	1200	2	500	2	900
6	1300	2	500	3	960
7	800	2	500	2	960
14	700	2	500	3	1080
16	600	2	500	1	1140
1	500	2	500	2	1200
2	600	2	500	2	1200

By applying the optimization procedure, demands are grouped into commands which are executed together using the same irradiated raw material – allowing thus to maximize the number of executed demands. The only constraints are: a single type of product can be executed at a given time, a maximum of 3.5 mL can be irradiated and if the raw material is irradiated for obtaining the highest activity. This means that less irradiated raw material is used for commands with lower activity. Thus, the advantage of production optimization is that it reduces the production cycles by combining demands into a single command. As can be seen from Fig.5 the demands can be grouped into 2 separate commands (command 1 with product type NaF, and command 2 with product type FDG) but there some demands that exceed the production intervals (marked with read).

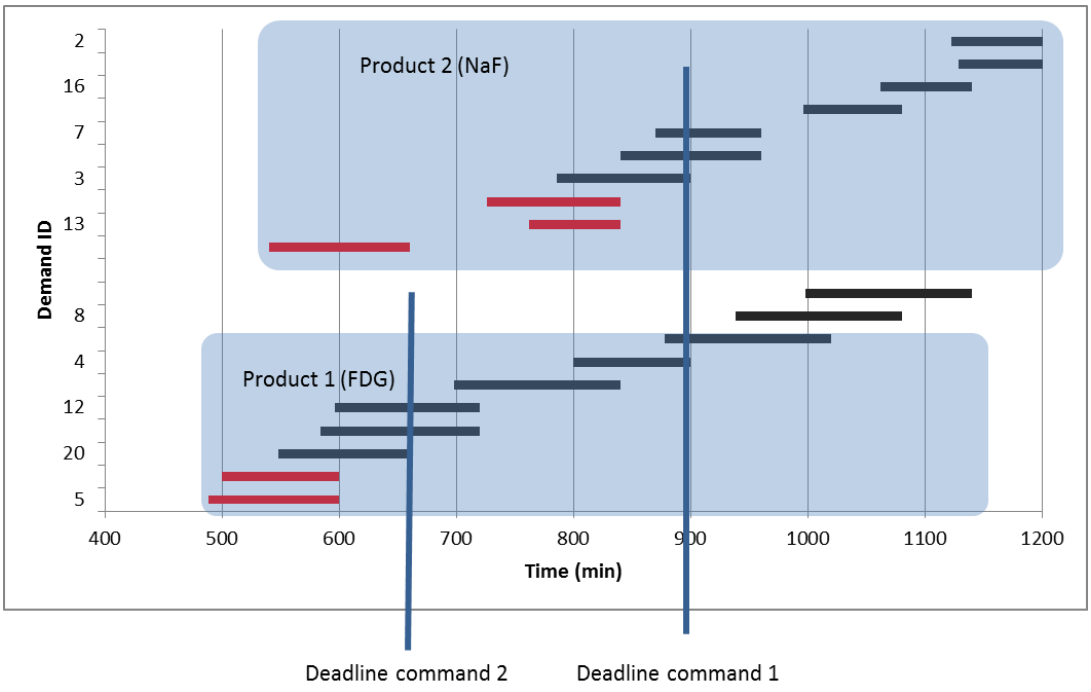

Fig. 5. Demand grouping with ILOG optimization

By running the optimization model on the specified data a set of 15 demands have been chosen for production as descripted in the above table (the entries in white have not been processed). The details of the optimization model are given below:

```
// solution with objective 15
initialQuantity  [500 500 500 500 500 500 500 500 500 500 500 5000
500 500 500 500 500 500 500 500]
diluted  [2.6 2.1667 1.0833 2 1.5556 1 1.625 1 2 1 1.0769 1.2727
2.1667 1.8571 1.0833
     2.1667 1 1 1 1.5556]
Where  [1 1 1 2 2 1 1 2 2 1 2 2 1 1 1 1 2 2 2 2]
Processed  [1 1 1 1 0 1 1 1 0 0 1 1 0 1 0 1 1 1 1 1]
command finish time  [900 660]
maxIrrAct  [1300 1400]
Load  [2192.3 3428.6]
Cyclotron execution time  [108 114]
Synthesis execution time  [7 23]
Dispense execution time  [23 23]
Execution time  [228 250]
Total execution time 478
Execution modes  [<1 672 900 228> <1 410 660 250>]
Command 1 produces 2192.307692307692 liquid of NaF type,
irradiated at 1300 for 900
```

```
the following demands are done in it:
Demand 1 with irradiation 500 diluted at 2.6. Needed at 1200
Demand 2 with irradiation 600 diluted at 2.166666666666667. Needed
at 1200
Demand 3 with irradiation 1200 diluted at 1.083333333333333.
Needed at 900
Demand 6 with irradiation 1300 diluted at 1. Needed at 960
Demand 7 with irradiation 800 diluted at 1.625. Needed at 960
Demand 14 with irradiation 700 diluted at 1.857142857142857.
Needed at 1080
Demand 16 with irradiation 600 diluted at 2.166666666666667.
Needed at 1140
Command 2 produces 3428.571428571428 liquid of FDG type,
irradiated at 1400 for 660
the following demands are done in it:
Demand 4 with irradiation 700 diluted at 2. Needed at 900
Demand 8 with irradiation 1400 diluted at 1. Needed at 1080
Demand 11 with irradiation 1300 diluted at 1.076923076923077.
Needed at 720
Demand 12 with irradiation 1100 diluted at 1.272727272727273.
Needed at 720
Demand 17 with irradiation 1400 diluted at 1. Needed at 1020
Demand 18 with irradiation 1400 diluted at 1. Needed at 1140
Demand 19 with irradiation 1400 diluted at 1. Needed at 840
Demand 20 with irradiation 900 diluted at 1.555555555555556.
Needed at 660
```

As a conclusion, based on the proposed scenario (Table 3) the automatic procedure using ILOG is better than the usage of production rules (15 accepted demands in the case of ILOG against 14 accepted demands in the case of production rules).

5. Conclusions

The higher irradiation currents available nowadays in modern cyclotrons allows more flexibility in scheduling, improved profitability, and reduced strain on the cyclotron when not operated at peak capacity. From the experimental data obtained we found out that the same activity (113 GBq) could be obtained either by 120 min session using 30 μA or with 60 min session using 50 μA. Since target lifetime is shortened at high beam current, a good compromise must be made between the produced activity and target degradation; the data obtained experimentally was used for planning (the session durations) and safe resource parameter configuring (irradiation current).

By comparing the results obtained in irradiation sessions with theoretical values [11] gives an excellent indication of beam fluency in the target medium.

These findings allowed shortening the total production time when deadline must be reached and to preserve equipment lifetime when lower orders are received.

Dual beam irradiation alongside high irradiation current may increase the production capacity of the nuclear facility from a local provider to a regional one. On the other hand, the tolerance to performance reduction of critical components to achieve high current operation is reduced at high irradiation currents. This may result in a lower safety margin of the critical components during beam irradiation, hence close monitoring of critical environment parameters by the environment automated control system – master over the holonic production control system is essential to maintain safe operations for the resources and the personnel involved.

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