Appl Intell (2008) 28: 261–274
DOI 10.1007/s10489-007-0070-2

Modeling adaptation of breast cancer treatment decision protocols in the KASIMIR project

Jean Lieber · Mathieu d'Aquin · Fadi Badra · Amedeo Napoli

Abstract Medical decision protocols constitute theories for health-care decision making that are applicable for "standard" medical cases but have to be adapted for the other cases. This holds in particular for the breast cancer treatment protocol studied in the KASIMIR research project. Protocol adaptations can be seen as knowledge-intensive case-based decision support processes. Some examples of adaptations that have been performed by oncologists are presented in this paper. Several issues are then identified that need to be addressed while trying to model such processes, namely: the complexity of adaptations, the lack of relevant information about the patient, the necessity to take into account the applicability and the consequences of a decision, the closeness to decision thresholds, and the necessity to consider some patients according to different viewpoints. As handling these issues requires some additional knowledge, which has to be acquired, different methods are presented that perform adaptation knowledge acquisition either from experts, or in a semi-automatic manner. A discussion and a conclusion end the paper.

Keywords Case-based decision support · Knowledge-intensive case-based reasoning · Breast cancer treatment · Medical informatics

1 Introduction

Protocols and guidelines are widely used in the medical domain [1, 2]. They indicate the standard way of taking care of patients. Unfortunately, they do not cover all the medical knowledge useful for health care: they constitute theories that have to be confronted with a practice showing a lot of exceptions. In particular, the protocol for breast cancer treatment is a document associating a treatment recommendation to a patient description. The direct application of the protocol only gives a satisfactory result for 60 to 70% of medical cases. It has been shown that, for the remaining medical cases, this protocol is in general *adapted* by physicians, meaning that it is not used in its current form, but that it is modified for these cases [3]. The modeling of protocol adaptations constitutes one of the research trends in the KASIMIR research project, holding on knowledge management and decision support in oncology. This paper presents a general overview of the researches on the modeling of these adaptations, from a computer science viewpoint. Thus, it consists in a synthesis of earlier work and discusses the issue of the integration of these contributions in a sole CBR architecture.

Section 2 introduces the KASIMIR project and shows in particular why a protocol adaptation can be considered a process of case-based reasoning (CBR [4]). Section 3

J. Lieber (✉) · M. d'Aquin · F. Badra · A. Napoli
Orpailleur team, LORIA (UMR 7503
CNRS-INPL-INRIA-Nancy 2-UHP), BP 239, 54 506,
Vandoeuvre-les-Nancy, France
e-mail: lieber@loria.fr

M. d'Aquin
e-mail: daquin@loria.fr

F. Badra
e-mail: badra@loria.fr

A. Napoli
e-mail: napoli@loria.fr

M. d'Aquin
Knowledge Media Institute (KMi), The Open University,
Milton Keynes, UK
e-mail: m.daquin@open.ac.uk

presents some examples of adaptations performed by domain experts and discussed during sessions of adaptation knowledge acquisition (AKA) from experts. Based on these examples, several issues related to protocol adaptation—and to CBR—are pointed out. Section 4 is the core of the paper and shows how these issues have been addressed and integrated in the KASIMIR project. The KASIMIR CBR system relies on domain-dependent adaptation knowledge and can be considered a knowledge-intensive CBR system [5]. Research on AKA for the KASIMIR system is presented in Sect. 5. Section 6 details the current state of the implementations within the KASIMIR system. Related work is disseminated throughout the paper. However, related work in CBR applied to medical applications is discussed in Sect. 7. Section 8 concludes the paper and presents ongoing and future work.

2 The KASIMIR project

2.1 Medical context

During the last decades, a huge research effort has been found on oncology. In particular, the research on breast cancer has led to improvements in its therapy. The negative side is that the elaboration of the best treatment for a specific patient, that should be based on the medical state of the art according to evidence-based medicine principles [6], has become very complex and evolves quickly. This is one reason that has motivated the writing of the breast cancer treatment protocol, simply called "the protocol" hereafter, i.e. a document compiling the researches on breast cancer treatment. The protocol explains which treatment should be proposed, given the patient description.

The protocol application is acceptable for only 60 to 70% of patients according to the experts involved in the KASIMIR project and to their everyday medical practice. This can be seen as an instance of the so-called qualification problem introduced in [7]: it is impossible to list all the specific situations that prevent from the application of the protocol. For the out of protocol patients, it has been shown in [3] that physicians adapt the protocol, meaning that they actually use the protocol with a critical eye modifying the recommendations. Some examples of protocol adaptations are given in Sect. 3. Actually, adaptations are usually performed during the so-called breast therapeutic decision meetings, that gather experts in each specialty involved in breast cancer treatment, i.e., surgery, chemotherapy, radiotherapy, etc.

The adaptations of the protocol can be seen as confrontations of a theory—the protocol—and a practice—the out of protocol medical cases. Not surprisingly, these confrontations have an effect on the theory: in [3], it has been shown that protocol adaptations may lead to protocol evolutions.

2.2 Application, adaptation and evolution of a medical protocol

The goal of the KASIMIR project is to provide tools for the management of decision knowledge in oncology. In this project are involved experts in oncology (in particular, from the *Centre Alexis Vautrin*, in Vandœuvre-lès-Nancy), physicians of the Lorraine region, in France (members of the health-care network Oncolor, www.oncolor.org), computer engineers (of Oncolor and of the Hermès association, www.hermes.asso.fr), researchers in computer science (of the Orpailleur team) and in psycho-ergonomics (of the *Laboratoire d'ergonomie du CNAM*, Paris). The existing and future tools for this knowledge management are implemented in the KASIMIR system. Developments in the KASIMIR system follow the decision-making structure used in cancer treatment; consists sig of three main stages: the application, adaptation, and the evolution of the protocol.

Protocol application The protocol application part of the KASIMIR system consists of the implementation of the protocol as a knowledge base. Two main versions have been implemented. The first one is based on an object knowledge representation formalism [8], and the second one relies on OWL DL, the part of the *Web Ontology Language* OWL [9] corresponding to the description logic $\mathcal{SHOIN}(\mathrm{D})$ [10]. In this last version [11], the KASIMIR system is implemented as a semantic portal, i.e. a portal of the semantic Web in which the knowledge bases as well as the querying and reasoning services are distributed on the Web [12]. Both systems are based on subsumption tests and hierarchical classification (see [8] for the principles of their implementations).

The protocol can be seen as a set of rules $\mathtt{R} = \mathtt{Pat} \rightarrow \mathtt{Ttt}$, where `Pat` represents a class of patients by the way of conditions on patient features (age, tumor size, etc.) and `Ttt` represents a treatment recommendation. Given `tgt`, the description of a target patient, the protocol application consists in searching the rule $\mathtt{R} = \mathtt{Pat} \rightarrow \mathtt{Ttt}$ such that if `tgt` fulfills the conditions of `Pat`—denoted by $\mathtt{Pat} \Leftarrow \mathtt{tgt}$ in the following—then `Ttt` is a therapeutic recommendation for `tgt`. $\Leftarrow$ is implemented by the subsumption test: $\mathtt{Pat} \Leftarrow \mathtt{tgt}$ if the set of patients represented by `Pat` contains the set of patients represented by `tgt` (`tgt` represents the patients having the same description as the target patient). `Ttt` is in general composed of several treatments corresponding to the main treatment categories (surgery, chemotherapy, etc.).

This part of the KASIMIR system is fully implemented and several protocols can be accessed on the Web (http://www.hermes.asso.fr/KasimirWeb) and are actually used by physicians.

Protocol adaptation It may occur that the protocol application does not lead to a satisfactory treatment for a given target patient $\mathtt{tgt}$. This means either that the protocol is incomplete (i.e., there is no $\mathtt{R} = \mathtt{Pat} \rightarrow \mathtt{Ttt}$ such that $\mathtt{Pat} \Leftarrow \mathtt{tgt}$) or that the treatment proposed involves some difficulties (e.g., the treatment is doubtful, it raises a contraindication, or it is inapplicable). Given $\mathtt{tgt}$, the KASIMIR module for protocol adaptation selects a protocol rule $\mathtt{R} = \mathtt{Pat} \rightarrow \mathtt{Ttt}$ and then adapts $\mathtt{Ttt}$ to solve $\mathtt{tgt}$. This can be seen as a CBR process, as shown in Sect. 2.3.

Protocol evolution Currently, this part of the KASIMIR project has not been investigated in detail, and nothing has been implemented yet. The objective is to work on adaptations actually performed during breast therapeutic decision meetings: not only on the descriptions of patients and treatments, but also on the representation of the adaptation processes. The extraction from these data of frequently performed adaptations may lead to potential protocol evolutions, to be integrated in the KASIMIR system.

2.3 Protocol adaptation and case-based decision support

Case-based reasoning: basic notions and notations Case-based reasoning (CBR) consists in solving a target problem $\mathtt{tgt}$ with the help of a set of source cases, called the case base, a source case being the representation of a problem-solving episode. In the following, a source case is denoted by an ordered pair $(\mathtt{srce}, \mathtt{Sol}(\mathtt{srce}))$ where $\mathtt{srce}$ is a *source problem* and $\mathtt{Sol}(\mathtt{srce})$ is a solution of $\mathtt{srce}$, called a *source solution* (other units of information may be associated with this pair). A classical decomposition of a CBR process consists in retrieval and adaptation steps. Retrieval consists in choosing a source case $(\mathtt{srce}, \mathtt{Sol}(\mathtt{srce}))$ such that $\mathtt{srce}$ is similar to $\mathtt{tgt}$, according to a similarity criterion. The adaptation operation aims at designing a solution $\mathtt{Sol}(\mathtt{tgt})$ of $\mathtt{tgt}$ in adapting $\mathtt{Sol}(\mathtt{srce})$.

Adaptation aims at solving $\mathtt{tgt}$ thanks to $(\mathtt{srce}, \mathtt{Sol}(\mathtt{srce}))$ and thus, leads to a solution of $\mathtt{tgt}$, denoted by $\mathtt{Sol}(\mathtt{tgt})$. Figure 1 illustrates the CBR process.

A variant of this CBR decomposition consists in searching several source cases and then, in combining them in order to solve the target problem (this second step is called the *combination step*).

$$\begin{tikzcd}
\mathtt{srce} \arrow[d] & & \mathtt{tgt} \arrow[ll, "\textit{Retrieval}"'] \arrow[d] \\
\mathtt{Sol}(\mathtt{srce}) \arrow[rr, "\textit{Adaptation}"'] & & \mathtt{Sol}(\mathtt{tgt})
\end{tikzcd}$$

Fig. 1 The CBR process: a source case $(\mathtt{srce}, \mathtt{Sol}(\mathtt{srce}))$ similar to $\mathtt{tgt}$ is retrieved in the case base and then is adapted to solve $\mathtt{tgt}$

Protocol adaptation and CBR The protocol adaptation described in the previous section can be seen as a CBR process if each of the rules $\mathtt{R} = \mathtt{Pat} \rightarrow \mathtt{Ttt}$ is considered to be a source case $(\mathtt{srce}, \mathtt{Sol}(\mathtt{srce}))$: $\mathtt{srce} = \mathtt{Pat}$ and $\mathtt{Ttt} = \mathtt{Sol}(\mathtt{srce})$. A particularity of the KASIMIR system is that source cases are "ossified" (according to the terminology of [4]) or "generalized" (according to the terminology of [13]): a source case is a compilation of a large set of specific medical cases. The solution of a problem is a recommendation and, as such, is a suggestion of a therapeutic decision. Hence, protocol adaptations can be seen as case-based decision support processes but based exclusively on prototypical cases.

3 Examples of protocol adaptations by domain experts

The examples presented in this section are based on the minutes of breast therapeutic decision meetings that were studied further, during the sessions of adaptation knowledge acquisition from experts. They have been simplified by removing pieces of information that are irrelevant to decision making, and some details have been changed, for anonymity reasons (e.g., patient names) or for the sake of simplicity.

The objective of this section is to point out, from these examples, issues on protocol adaptations.

3.1 Example 1: case of a man with a breast cancer

The breast cancer protocol has been written by experts according to evidence-based medicine principles, based on medical publications that present results from statistical studies. The large majority of medical cases (about 99%) corresponds to female patients, and this explains why the protocol is written for women.

Now, let us consider the medical case of Jules, a man suffering from a cancer at the left breast. The protocol cannot be applied because of the gender of Jules and also because the localization of the tumor in the breast is unknown (which is actually a consequence of the gender: the anatomy of a woman breast cannot be mapped into the anatomy of a man breast in a way relevant to decision making).

The principle of the adaptation performed by the physicians can be understood as applying the protocol to the extent possible. The fact that Jules is a man is temporarily neglected (he is considered as a woman Julie) and the protocol recommends, knowing other features of Jules not detailed here, a partial breast ablation (surgery), a FEC 50 chemotherapy (FEC is composed of three drugs and 50 is a dose), and an ovary ablation (hormone therapy) but does not recommend a radiotherapy, since the kind of radiotherapy that is to be proposed depends on the tumor localization. Both the surgery and the chemotherapy can be efficiently applied as such for Jules. The parts of the treatment that require some adaptation are the hormone therapy and the radiotherapy.

The problem with the hormone therapy that is proposed by the protocol for Julie—ovary ablation—is that it cannot be applied to Jules, for obvious reasons. The adaptation consists in replacing it with another hormone therapy, having similar effects. In the case of Jules, a cure of tamoxifen (a hormone therapy drug) is chosen.

The problem with radiotherapy is that it is not known whether (*a*) the tumor localization is—or can be considered as—external or (*b*) non external (i.e., internal or central). If (*a*) (resp., (*b*)) holds for Jules, a radiotherapy $\mathtt{rad}_{(a)}$ (resp., $\mathtt{rad}_{(b)}$) is recommended by the protocol. The radiotherapy act following decision $\mathtt{rad}_{(b)}$ is the same as the one following decision $\mathtt{rad}_{(a)}$, except that some technical additional precautions are taken in order to avoid irradiating the internal mammary chain. If it is considered better to take precautions even if they are unnecessary, then decision $\mathtt{rad}_{(b)}$ has to be taken.

The three following issues about protocol adaptation can be pointed out:

- *The complexity of protocol adaptations*: in the example, there are two reasons for adapting the protocol—one being a consequence of the other. In general, a protocol adaptation depends on several reasons, involving a complex adaptation that, to be computable, requires it to be decomposed into simpler operations.
- *The management of lacking information about the target problem*: in the example, the tumor localization is unknown and the missing information is necessary for solving the target problem. Similar situations have occurred during AKA from experts sessions, and the need to model therapeutic decision making when information is missing has emerged.
- *Adaptations of decision protocols involve features of decision making theory*, such as the applicability of a decision, its positive (expected) and negative (undesirable) consequences: in the example, ovary ablation is a decision that is not applicable and that is replaced with a decision having similar consequences.

3.2 Example 2: case of a patient with an age close to a decision threshold

Some features of breast cancer cases are numerical, as, for example, the age of the patient or the size of the tumor. A condition on a protocol rule holding on such a feature f is generally of the form $f < \tau$, $f \leq \tau$, $f \geq \tau$, or $f > \tau$, where τ is a numerical threshold. For example, let $(\mathtt{srce}_1, \mathtt{Sol}(\mathtt{srce}_1))$ and $(\mathtt{srce}_2, \mathtt{Sol}(\mathtt{srce}_2))$ be two source cases (two protocol rules) defined by

$$\mathtt{srce}_1 = C \wedge \mathtt{age} < 40,$$
$$\mathtt{Sol}(\mathtt{srce}_1) = \{\mathtt{FEC\text{-}100}, \mathtt{tamoxifen}\},$$
$$\mathtt{srce}_2 = C \wedge \mathtt{age} \geq 40, \qquad \mathtt{Sol}(\mathtt{srce}_2) = \{\mathtt{FEC\text{-}100}\}$$

where C is a conjunction of conditions: female gender, nodal status negative, hormone receptor status positive, tumor grade 1, $\mathtt{age} < 70$, and tumor size of less than 2 cm; `FEC-100` is a chemotherapy recommendation, and `tamoxifen` is a drug for hormone therapy.

Let Fernande denote a 42 year old patient satisfying the conditions in C. A straightforward application of the protocol leads to the recommendation $\mathtt{Sol}(\mathtt{srce}_2)$, since $\mathtt{srce}_2 \Leftarrow$ Fernande. However, this application of the protocol is questionable. Indeed, the precision in the choice of the threshold when the protocol was established is rather low: it could have been as well 37 or 43. Moreover, a patient of 42 years that has a good health excepting her cancer could be considered with an age lower than 40, from a medical viewpoint. From discussions with the experts, it seems that this threshold should be considered with a precision of ±5 years, meaning that if condition $C \wedge \mathtt{age} < 35$ (resp., $C \wedge \mathtt{age} > 45$) holds for a patient, then the age of this patient does not make the decision $\mathtt{Sol}(\mathtt{srce}_1)$ (resp., $\mathtt{Sol}(\mathtt{srce}_2)$) questionable. By contrast, for Fernande, both solutions $\mathtt{Sol}(\mathtt{srce}_1)$ and $\mathtt{Sol}(\mathtt{srce}_2)$ could be proposed, with a preference for the second one, since the age of Fernande is higher than the threshold 40. This is the cautious policy chosen for KASIMIR, knowing that the user could go further: he/she can make a choice or a combination of solutions. Here, an acceptable combination could be to keep the `FEC-100` treatment (proposed in both solutions) and to recommend tamoxifen with a lower dose than the standard.

The following issue can be pointed out:

- *The closeness to a decision threshold* may lead to a choice between several solutions (or to a combination of them), even for a "standard patient": though Fernande is not (formally) out of the protocol, there are two relevant decision protocol rules for her.

3.3 Example 3: case of a tumor in a small breast

The protocol is written for "standard patients", having features that are close to the average. A patient with a feature that is not standard may involve a protocol adaptation.

For example, Marcelle is a patient with a tumor of size $S_{\text{tumor}} = 3$ cm in her right breast. A feature making Marcelle non standard is that the size of her breast is small, compared to the average. This feature does not affect neither chemotherapy, nor radiotherapy, nor hormone therapy:

according to these treatment categories, the protocol can be applied in a straightforward manner to Marcelle. But for surgery, this feature is important, as explained hereafter.

The choice of a surgery according to protocol depends in particular on the tumor size S_{tumor}: given other conditions on patients, if $S_{\text{tumor}} < 4$ cm then a partial mastectomy is recommended, else a radical mastectomy is recommended. A partial mastectomy is a conservative treatment: it removes only a part of the breast (the tumor and a margin of resection), and then, the shape of the breast can be reconstructed. A radical mastectomy is non conservative: it removes the whole breast.

A straightforward application of the protocol to Marcelle leads to a partial mastectomy, but, since her breast is too small, this conservative surgery is not applicable in practice. Therefore, a radical mastectomy is recommended for Marcelle.

The idea of this adaptation is that *for surgery*, the size of the tumor is considered relatively to the size of the breast: the surgical decision is taken for Marcelle *as if* Marcelle had a larger tumor (say, of size $S_{\text{tumor}} = 5$ cm) in a breast of standard size. By contrast, from the viewpoints of chemotherapy, radiotherapy, and hormone therapy, the tumor is considered as a $S_{\text{tumor}} = 3$ cm tumor: its size is considered as an absolute value, not to be taken relatively to the breast size.

The following issue can be pointed out:

- *The patient may have to be considered according to several viewpoints:* in the example, two different values—3 and 5 cm—for the tumor size are considered. Each value is meaningful in a certain viewpoint: 5 cm, according to the surgery viewpoint, 3 cm, according to, e.g., the chemotherapy viewpoint.

4 Modeling protocol adaptations as CBR processes

The above examples above have pointed out several issues about protocol adaptation. This section shows how they are modeled for the KASIMIR CBR system:

- Some protocol adaptations are complex and have to be decomposed into simple adaptation steps (Sect. 4.1);
- Some features of the patient that are relevant to the decision making may be missing (Sect. 4.2);
- Decision protocol adaptation are often based on the study of the applicability and of the consequences of a decision (Sect. 4.3);
- Closeness to a threshold has a direct influence on the retrieval of similar cases (Sect. 4.4);
- A patient has to be considered according to several viewpoints (Sect. 4.5).

The solutions of these issues have to be integrated; this is discussed in Sect. 4.6.

4.1 Decomposition of complex adaptations into adaptation paths

Let us consider the example of Sect. 3.1 (case of a man with a breast cancer). There are two main reasons for adapting the protocol for Jules. The modeling consists first in introducing *virtual patients* by neglecting temporarily these reasons, in order to be in accordance with the protocol. What we call a "virtual patient" is the description of a patient that does not necessarily correspond to an actual patient and that is introduced as an intermediary between the target patient and the protocol.

The first reason making Jules an out of protocol medical case is the gender. Thus, let Julie be a (virtual) woman having the same features as Jules, except the gender. This may be represented by a relation "Julie $\mathtt{cg}$ Jules", where "$\mathtt{cg}$" is the binary relation "has an equivalent description, except for the change of gender."

Julie has a tumor in the left breast with an unknown localization: (a) external or (b) internal or central. Let Julie $\wedge\,(a)$ and Julie $\wedge\,(b)$ be the two virtual patients having the same features as Julie, with Julie $\wedge\,(a)$ verifying the feature (a) and Julie $\wedge\,(b)$, verifying the feature (b). The relation between Julie $\wedge\,(a)$ (resp. Julie $\wedge\,(b)$) and Julie is denoted by $\Rightarrow$: Julie $\wedge\,(a) \Rightarrow$ Julie and Julie $\wedge\,(b) \Rightarrow$ Julie.

For both Julie $\wedge\,(a)$ and Julie $\wedge\,(b)$, the protocol provides recommendations: there are two source cases (i.e., two protocol rules) $(\mathtt{srce}_{(a)}, \mathtt{Sol}(\mathtt{srce}_{(a)}))$ and $(\mathtt{srce}_{(b)}, \mathtt{Sol}(\mathtt{srce}_{(b)}))$ such that $\mathtt{srce}_{(a)} \Leftarrow$ Julie $\wedge\,(a)$ and $\mathtt{srce}_{(b)} \Leftarrow$ Julie $\wedge\,(b)$, meaning that Julie $\wedge\,(a)$ satisfies $\mathtt{srce}_{(a)}$ and Julie $\wedge\,(b)$ satisfies $\mathtt{srce}_{(b)}$.

Therefore, Jules can be related to two source problems, $\mathtt{srce}_{(a)}$ and $\mathtt{srce}_{(b)}$. These two relationships are reified into two *similarity paths*:

$$\mathtt{srce}_{(a)} \quad \Leftarrow \quad \text{Julie} \wedge (a) \quad \Rightarrow \quad \text{Julie} \quad \mathtt{cg} \quad \text{Jules} \tag{1}$$

$$\mathtt{srce}_{(b)} \quad \Leftarrow \quad \text{Julie} \wedge (b) \quad \Rightarrow \quad \text{Julie} \quad \mathtt{cg} \quad \text{Jules} \tag{2}$$

More generally, a similarity path from a problem $\mathtt{srce}$ to a problem $\mathtt{tgt}$ is a sequence of the form

$$\mathtt{pb}_0 \quad \mathtt{r}_1 \quad \mathtt{pb}_1 \quad \mathtt{r}_2 \quad \mathtt{pb}_2 \quad \ldots \quad \mathtt{pb}_{q-1} \quad \mathtt{r}_q \quad \mathtt{pb}_q \tag{3}$$

where $\mathtt{pb}_0 = \mathtt{srce}$, $\mathtt{pb}_q = \mathtt{tgt}$, the $\mathtt{pb}_i$s for $1 \le i \le q-1$ are *intermediate problems* (problems introduced for the purpose of reasoning), and the $\mathtt{r}_i$s for $1 \le i \le q$ are binary relations between problems (such as $\Leftarrow$, $\Rightarrow$, and $\mathtt{cg}$). The main property of a relation $\mathtt{r}$ involved in a similarity path is that $\mathtt{r}$ is associated with an *adaptation function* $\mathcal{A}_{\mathtt{r}}$: $\mathtt{r}$ relates two elements of the problem space and $\mathcal{A}_{\mathtt{r}}$, two elements of the solution space. A pair $(\mathtt{r}, \mathcal{A}_{\mathtt{r}})$ is called a *reformulation* and

$$\begin{tikzcd}
\mathtt{srce} = \mathtt{pb}_0 \arrow[r, dash, "\mathtt{r}_1"] \arrow[d] & \mathtt{pb}_1 \arrow[r, dash, "\mathtt{r}_2"] \arrow[d] & \mathtt{pb}_2 \arrow[r, dash, "\dots"] \arrow[d] & \mathtt{pb}_{q-1} \arrow[r, dash, "\mathtt{r}_q"] \arrow[d] & \mathtt{pb}_q = \mathtt{tgt} \arrow[d] \\
\mathtt{Sol}(\mathtt{srce}) = \mathtt{Sol}(\mathtt{pb}_0) \arrow[r, dash, "\mathcal{A}_{\mathtt{r}_1}"'] & \mathtt{Sol}(\mathtt{pb}_1) \arrow[r, dash, "\mathcal{A}_{\mathtt{r}_2}"'] & \mathtt{Sol}(\mathtt{pb}_2) \arrow[r, dash, "\dots"'] & \mathtt{Sol}(\mathtt{pb}_{q-1}) \arrow[r, dash, "\mathcal{A}_{\mathtt{r}_q}"'] & \mathtt{Sol}(\mathtt{pb}_q) = \mathtt{Sol}(\mathtt{tgt})
\end{tikzcd}$$

Fig. 2 A similarity path and the associated adaptation path

corresponds to the following adaptation rule:

> **if** $\mathtt{pb}$ and $\mathtt{pb}'$ are two problems such that $\mathtt{pb}\ \mathtt{r}\ \mathtt{pb}'$
> and $\mathtt{Sol}(\mathtt{pb})$ is a solution of $\mathtt{pb}$
> **then** $\mathtt{Sol}(\mathtt{pb}') = \mathcal{A}_{\mathtt{r}}(\mathtt{pb}, \mathtt{Sol}(\mathtt{pb}), \mathtt{pb}')$
> is a solution of $\mathtt{pb}'$.

Therefore, if a similarity path (3) is established between $\mathtt{pb}_0 = \mathtt{srce}$ and $\mathtt{pb}_q = \mathtt{tgt}$, then $\mathtt{Sol}(\mathtt{pb}_0) = \mathtt{Sol}(\mathtt{srce})$ can be adapted in a solution $\mathtt{Sol}(\mathtt{pb}_q) = \mathtt{Sol}(\mathtt{tgt})$ by applying in sequence $\mathcal{A}_{\mathtt{r}_1}, \mathcal{A}_{\mathtt{r}_2}, \dots, \mathcal{A}_{\mathtt{r}_q}$:

$$\begin{aligned}
&\mathtt{Sol}(\mathtt{pb}_1) = \mathcal{A}_{\mathtt{r}_1}(\mathtt{pb}_0, \mathtt{pb}_1, \mathtt{Sol}(\mathtt{pb}_0)),\\
&\mathtt{Sol}(\mathtt{pb}_2) = \mathcal{A}_{\mathtt{r}_2}(\mathtt{pb}_1, \mathtt{pb}_2, \mathtt{Sol}(\mathtt{pb}_1)),\\
&\qquad\vdots\\
&\mathtt{Sol}(\mathtt{pb}_q) = \mathcal{A}_{\mathtt{r}_q}(\mathtt{pb}_{q-1}, \mathtt{pb}_q, \mathtt{Sol}(\mathtt{pb}_{q-1}))
\end{aligned} \tag{4}$$

(4) is called the *adaptation path* following the similarity path (3). Figure 2 illustrates the notions of similarity and adaptation paths and can be seen as an instantiation of Fig. 1.

The adaptation paths following the similarity paths (1) and (2) are based on the reformulations $(\Leftarrow, \mathcal{A}_{\Leftarrow})$, $(\Rightarrow, \mathcal{A}_{\Rightarrow})$, and $(\mathtt{cg}, \mathcal{A}_{\mathtt{cg}})$. The reformulation $(\Leftarrow, \mathcal{A}_{\Leftarrow})$ corresponds to the direct application of the protocol: $\mathtt{Sol}(\mathtt{pb}_1) = \mathtt{Sol}(\mathtt{pb}_0)$. $(\Rightarrow, \mathcal{A}_{\Rightarrow})$ is studied in Sect. 4.2, and $(\mathtt{cg}, \mathcal{A}_{\mathtt{cg}})$ in Sect. 4.3. These adaptation processes lead to two different recommendations for Jules. A preference between the recommendations is established and discussed in Sect. 4.2.

From an implementation viewpoint, given a case base, a set of reformulations constituting the adaptation knowledge, and a target problem $\mathtt{tgt}$, the CBR approach consists firstly in finding a source case $(\mathtt{srce}, \mathtt{Sol}(\mathtt{srce}))$ with a similarity path from $\mathtt{srce}$ to $\mathtt{tgt}$, and secondly in following this similarity path in the solution space. The second operation is simple, from an algorithmic viewpoint: it consists in processing the adaptation path (4). The first operation is a search in the problem space structured by the relations $\mathtt{r}$. To each step $\mathtt{pb}\ \mathtt{r}\ \mathtt{pb}'$ of a similarity path, a numerical cost $\mathtt{cost}(\mathtt{pb}\ \mathtt{r}\ \mathtt{pb}')$ is associated: basically, $\mathtt{cost}(\mathtt{pb}\ \mathtt{r}\ \mathtt{pb}')$ measures the adaptation effort performed by $\mathcal{A}_{\mathtt{r}}$, e.g., a measure of the risk of accepting as such the solution $\mathtt{Sol}(\mathtt{pb}') = \mathcal{A}_{\mathtt{r}}(\mathtt{pb}, \mathtt{pb}', \mathtt{Sol}(\mathtt{pb}))$, under the assumption that $\mathtt{Sol}(\mathtt{pb})$ is correct. The *length* of a similarity path (3) is $\sum_{i=1}^{q} \mathtt{cost}(\mathtt{pb}_{i-1}\ \mathtt{r}_i\ \mathtt{pb}_i)$. The distance $\mathtt{dist}(\mathtt{srce}, \mathtt{tgt})$ between $\mathtt{srce}$ and $\mathtt{tgt}$ is the length of the shortest similarity path from $\mathtt{srce}$ to $\mathtt{tgt}$. $(\mathtt{srce}, \mathtt{Sol}(\mathtt{srce}))$ is retrieved if it minimizes $\mathtt{dist}(\mathtt{srce}, \mathtt{tgt})$.

For KASIMIR, each $\mathtt{r}$ corresponds to a production rule: $\mathtt{pb}\ \mathtt{r}\ \mathtt{pb}'$ if $\mathtt{pb}$ can be produced from $\mathtt{pb}'$ by this rule. An A* search with an evaluation function based on the sum of the $\mathtt{cost}(\mathtt{pb}_{i-1}\ \mathtt{r}_i\ \mathtt{pb}_i)$ enables to find the shortest path from a given $\mathtt{srce}$ to $\mathtt{tgt}$. A combination of A* search and hierarchical classification, called *smooth classification*, allows to find the closest source case according to $\mathtt{dist}$, with the corresponding similarity path. The A* search is exponential in the worst case and the hierarchical classification is useful in particular to prune an important part of the search space. When the order between two relations $\mathtt{r}_1$ and $\mathtt{r}_2$ in a similarity path has an influence on the adapted solution, then two solutions of $\mathtt{tgt}$, associated with two adaptation paths, are proposed to the user.

The notions of similarity and adaptation paths have emerged from an application of CBR to synthesis planning in organic chemistry [14, 15], and the notion of reformulation has been introduced by Erica Melis [16, 17]. The algorithm for smooth classification can be found in [18]. It can be noticed that this CBR approach is consistent with the principle of adaptation-guided retrieval [19]: a retrieved source case is necessarily adaptable to solve the target problem.

4.2 Case-based decision support when information is missing

In the example of Sect. 3.1, information is missing about the patient Julie: it is not known whether the tumor is (*a*) external or (*b*) non external. Depending on (*a*) or on (*b*), the protocol recommends different decisions. In absence of information, the choice is finally made on the basis of the worst possible consequences (to be avoided) of these decisions.

This is an instance of what is called the *Wald pessimistic criterion* in [20] (and *minimax strategy* in [21]), that is explained hereafter. Let $\mathcal{C}$ be the finite set of possible consequences of decisions and $\geq^{\mathcal{C}}$, the total ordering on $\mathcal{C}$ such that $\mathtt{csq}_1 \geq^{\mathcal{C}} \mathtt{csq}_2$ is interpreted as "$\mathtt{csq}_1$ is preferred to $\mathtt{csq}_2$". Let $\mathtt{pb}$ be a decision problem; $\mathtt{pb}$ represents a class $\mathcal{I}(\mathtt{pb})$ of problem instances. Let $\mathtt{dec}$ be a decision and $\mathcal{C}(\mathtt{dec}, \mathtt{pb}) \subseteq \mathcal{C}$ be the set of the possible consequences following the decision $\mathtt{dec}$ in the context of the problem $\mathtt{pb}$: $\mathcal{C}(\mathtt{dec},\mathtt{pb})$ is the set of the consequences of $\mathtt{dec}$ on every problem instance $i \in \mathcal{I}(\mathtt{pb})$. Let $\mathtt{wpc}(\mathtt{dec},\mathtt{pb}) = \min \mathcal{C}(\mathtt{dec},\mathtt{pb})$ (according to $\leq^{\mathcal{C}}$): $\mathtt{wpc}(\mathtt{dec},\mathtt{pb})$ is the worst possible consequence of a decision $\mathtt{dec}$, in the context of $\mathtt{pb}$. According to the Wald pessimistic criterion, decision $\mathtt{dec}$ has to be preferred to decision $\mathtt{dec}'$, in the context of $\mathtt{pb}$, if $\mathtt{wpc}(\mathtt{dec},\mathtt{pb}) >^{\mathcal{C}} \mathtt{wpc}(\mathtt{dec}',\mathtt{pb})$: the worst possible consequence of $\mathtt{dec}$ is better than that of $\mathtt{dec}'$ and thus has to be preferred.

This can be applied to case-based decision support as follows. Let $\mathtt{pb}$ be a decision problem, (a) be an additional information and (b) be the negation of (a). Let $\mathtt{dec}$ be a decision. It can be shown that

$$\mathtt{wpc}(\mathtt{dec},\mathtt{pb}) = \min\{\mathtt{wpc}(\mathtt{dec},\mathtt{pb}\wedge(a)), \mathtt{wpc}(\mathtt{dec},\mathtt{pb}\wedge(b))\} \tag{5}$$

Let $\mathtt{dec}_{(a)}$ and $\mathtt{dec}_{(b)}$ be the decisions inferred by a reasoning process for $\mathtt{pb}\wedge(a)$ and $\mathtt{pb}\wedge(b)$. If $\mathtt{dec}_{(a)} \neq \mathtt{dec}_{(b)}$, this means that the information units (a) and (b) are relevant to solve $\mathtt{pb}$. In this situation, if $\mathtt{wpc}(\mathtt{dec}_{(b)},\mathtt{pb}) >^{\mathcal{C}} \mathtt{wpc}(\mathtt{dec}_{(a)},\mathtt{pb})$ then the Wald pessimistic criterion gives the preference to $\mathtt{dec}_{(b)}$. According to 5, it comes that $\mathtt{dec}_{(x)}$ has to be preferred for

$$x = \operatorname*{argmax}_{x\in\{a,b\}} \min_{y\in\{a,b\}} \mathtt{wpc}(\mathtt{dec}_{(x)},\mathtt{pb}\wedge(y)) \tag{6}$$

Therefore, when two solutions $\mathtt{Sol}_{(a)}(\mathtt{pb})$ and $\mathtt{Sol}_{(b)}(\mathtt{pb})$ of $\mathtt{pb}$ are proposed by two case-based decision support processes, they can be combined into a solution $\mathtt{Sol}(\mathtt{pb})$ according to preferences between the decisions $\mathtt{dec}_{(a)} \in \mathtt{Sol}_{(a)}(\mathtt{pb})$ and $\mathtt{dec}_{(b)} \in \mathtt{Sol}_{(b)}(\mathtt{pb})$.

In practice, for computing x according to (6), two additional assumptions have to be made. Firstly, among the four terms $\mathtt{wpc}(\mathtt{dec}_{(x)},\mathtt{pb}\wedge(y))$, the two terms corresponding to $x = y = a$ or $x = y = b$ can be removed if it is assumed that, for each $x \in \{a, b\}$ and for each decision $\mathtt{dec}'$:

$$\mathtt{wpc}(\mathtt{dec}_{(x)},\mathtt{pb}\wedge(x)) \geq^{\mathcal{C}} \mathtt{wpc}(\mathtt{dec}',\mathtt{pb}\wedge(x))$$

meaning that the decision $\mathtt{dec}_{(x)}$ is optimal in the context of $\mathtt{pb}\wedge(x)$ according to the Wald pessimistic criterion, which is a reasonable assumption when $\mathtt{dec}_{(x)}$ is a decision recommended by the protocol for $\mathtt{pb}\wedge(x)$. The second assumption is that the order between $\mathtt{wpc}(\mathtt{dec}_{(a)},\mathtt{pb}\wedge(b))$ and $\mathtt{wpc}(\mathtt{dec}_{(b)},\mathtt{pb}\wedge(a))$ either is known by the CBR system or can be retrieved from the user and retained for future reuse (this is what Kristian J. Hammond calls *learning by remembering* [22]).

This can be read in the current example as follows:

$$\mathtt{pb} = \text{Julie}, \quad (a) = \text{external}, \quad (b) = \neg(a),$$
$$\mathtt{dec}_{(a)} = \mathtt{rad}_{(a)}, \quad \mathtt{dec}_{(b)} = \mathtt{rad}_{(b)},$$

$$\mathtt{wpc}(\mathtt{dec}_{(a)},\mathtt{pb}\wedge(b)) = \text{“Consequence of a radiotherapy without precaution on a non external tumor”},$$

$$\mathtt{wpc}(\mathtt{dec}_{(b)},\mathtt{pb}\wedge(a)) = \text{“Consequence of a radiotherapy with unnecessary precautions”},$$

$$\mathtt{wpc}(\mathtt{dec}_{(b)},\mathtt{pb}\wedge(a)) >^{\mathcal{C}} \mathtt{wpc}(\mathtt{dec}_{(a)},\mathtt{pb}\wedge(b)).$$

The reformulation $(\Rightarrow, \mathcal{A}_{\Rightarrow})$ is defined by $\mathtt{pb} \Rightarrow \mathtt{pb}'$ if $\mathtt{pb}$ is a specialization of $\mathtt{pb}'$, $\mathcal{A}_{\Rightarrow}$ corresponds to a simple copy: the solution of $\mathtt{Sol}(\mathtt{pb})$ is applied to $\mathtt{pb}'$, but this copy may involve a risk. The use of the Wald pessimistic criterion as presented above allows to make a preference in order to minimize this risk.

This approach is still under study and should still be investigated more deeply, in particular for addressing its strengths and limitations.

4.3 Adaptation patterns for case-based decision support

Making a decision is choosing or designing an action that modifies the state of the world. A therapeutic decision, for example, leads to a treatment modifying the state of the patient. An action (and, by extension, a decision) may be applicable or not, and may have positive and/or negative consequences.

In the example of Sect. 3.1, the hormone therapy recommended by the protocol for Jules (when he is temporarily considered as a woman) is ovary ablation. This non applicable treatment is replaced with a cure of tamoxifen which has similar expected consequences for Jules as ovary ablation if Jules was a woman (i.e., for Julie).

This is an example of adaptation of an inapplicable decision. Such an adaptation can be realized with the help of the *adaptation pattern* of Fig. 3. The adaptation of the ovary ablation for Jules instantiates this pattern with:

$\underline{\mathtt{dec}}$ = ablation of the ovaries,

$\underline{\mathtt{dec}'}$ = tamoxifen,

$\underline{\mathtt{R}}$ = men have no ovaries.

This instantiation can be seen as an element of the reformulation $(\mathtt{cg}, \mathcal{A}_{\mathtt{cg}})$ introduced in Example 4.1: this element explains how an ovary ablation can be adapted to a man. The other elements of $(\mathtt{cg}, \mathcal{A}_{\mathtt{cg}})$ contain knowledge units such as “if $\mathtt{pb}\ \mathtt{cg}\ \mathtt{pb}'$, then the surgery, chemotherapy, and radiotherapy of $\mathtt{Sol}(\mathtt{pb})$ can be reused for $\mathtt{Sol}(\mathtt{pb}')$.” The adaptation pattern adds explanations that are useful to accept or reject an adaptation with a full knowledge of the facts, which is particularly important for a medical application.

In [23], two other adaptation patterns for case-based decision support are presented and exemplified by concrete

Parameters $\underline{\texttt{dec}}$, $\underline{\texttt{dec}'}$: two decisions having similar positive consequences when they are applicable and $\underline{\texttt{R}}$: a reason why a decision is not applicable

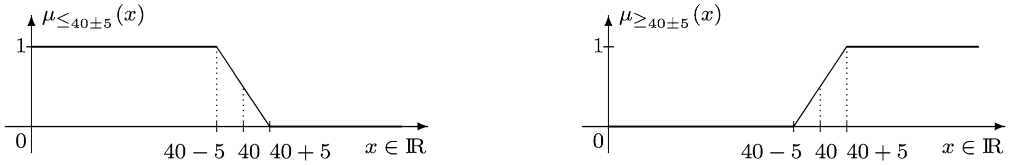
If $\underline{\texttt{dec}} \in \texttt{Sol}(\texttt{srce})$ **and** $\underline{\texttt{dec}}$ is not applicable (or difficult to apply) to $\texttt{tgt}$ because of $\underline{\texttt{R}}$ **and** $\underline{\texttt{dec}'}$ is applicable on $\texttt{tgt}$

then replace $\underline{\texttt{dec}}$ by $\underline{\texttt{dec}'}$ in $\texttt{Sol}(\texttt{srce})$ for obtaining $\texttt{Sol}(\texttt{tgt})$:

$$\texttt{Sol}(\texttt{tgt}) = (\texttt{Sol}(\texttt{srce}) \setminus \{\underline{\texttt{dec}}\}) \cup \{\underline{\texttt{dec}'}\}$$

Explanation The decision $\underline{\texttt{dec}}$ being non applicable to $\texttt{tgt}$ because of $\underline{\texttt{R}}$, it can be replaced by $\underline{\texttt{dec}'}$ that is applicable, and leads to positive consequences on $\texttt{tgt}$ similar to the ones of $\underline{\texttt{dec}}$ on $\texttt{srce}$.

Fig. 3 An adaptation pattern for an inapplicable decision



$$\mu_{\leq_{40\pm5}}(x) = \begin{cases} 1 & \text{if } x \leq 35 \\ \dfrac{45-x}{10} & \text{if } 35 < x < 45 \\ 0 & \text{if } x \geq 45 \end{cases} \qquad \mu_{\geq_{40\pm5}}(x) = 1 - \mu_{\leq_{40\pm5}}(x)$$

Fig. 4 The membership functions of the fuzzy sets $\leq_{40\pm5}$ and $\geq_{40\pm5}$

examples of the breast cancer treatment domain. There are linked with other aspects of decision support, in particular with the study of the consequences of a decision. They are adaptation patterns for:

- Treatments producing negative consequences—undesirable effects—such as treatments that are contraindicated for the current patient (drug contraindication because of another disease or because of the treatment of another disease, surgery problems because of troubles with blood coagulation, etc.);
- Treatments having insufficient positive consequences (compared to what is expected for a "standard patient").

The adaptation of a decision having at the same time too many negative consequences and insufficient positive consequences can be realized by combining these two patterns (in an adaptation path with two reformulations).

4.4 Use of fuzzy thresholds

For Fernande (cf. Sect. 3.2), since her age (42 years) is close to the decision threshold of 40, it is expected that both solutions $\texttt{Sol}(\texttt{srce}_1)$ and $\texttt{Sol}(\texttt{srce}_2)$ corresponding respectively to conditions $\texttt{age} < 40$ and $\texttt{age} \geq 40$ are proposed, with a preference for the latter. Indeed, it is considered that for $35 < \texttt{age} < 45$, both solutions are acceptable, with a preference for $\texttt{Sol}(\texttt{srce}_1)$ (resp., to $\texttt{Sol}(\texttt{srce}_2)$) for $\texttt{age} < 40$ (resp., $\texttt{age} > 40$). This can be modeled by replacing in the protocol the threshold 40 with a *fuzzy threshold*: instead of the two (crisp) sets $]-\infty; 40[$ and $[40; +\infty[$, the two fuzzy sets $\leq_{40\pm5}$ and $\geq_{40\pm5}$ whose membership functions $\mu_{\leq_{40\pm5}}$ and $\mu_{\geq_{40\pm5}}$ are represented on Fig. 4 are considered. This means that the two source problems $\texttt{srce}_1$ and $\texttt{srce}_2$ which represent crisp sets of patients—are replaced with $\mathcal{F}\texttt{srce}_1$ and $\mathcal{F}\texttt{srce}_2$—which represent fuzzy sets of patients. More precisely, let p, be a patient. If the (crisp) condition C does not hold for p, then $\mu_{\mathcal{F}\texttt{srce}_1}(p) = \mu_{\mathcal{F}\texttt{srce}_2}(p) = 0$. Else, if a is the age of p, then $\mu_{\mathcal{F}\texttt{srce}_1}(p) = \mu_{\leq_{40\pm5}}(a)$ and $\mu_{\mathcal{F}\texttt{srce}_2}(p) = \mu_{\geq_{40\pm5}}(a)$. The recommendation that is made is the set of solutions $\texttt{Sol}(\texttt{srce})$ of (possibly) fuzzified source problems $\mathcal{F}\texttt{srce}$, such that the target patient $\texttt{tgt}$ verifies $\mu_{\mathcal{F}\texttt{srce}}(\texttt{tgt}) > 0$. These solutions can be ranked with a decreasing value of these degrees.

For $\texttt{tgt}$ = Fernande, $\mu_{\mathcal{F}\texttt{srce}_1}(\texttt{tgt}) = 0.3$ and $\mu_{\mathcal{F}\texttt{srce}_2}(\texttt{tgt}) = 0.7$. Thus, the recommendation is $\texttt{Sol}(\texttt{srce}_1)$ or $\texttt{Sol}(\texttt{srce}_2)$, with a preference for the latter (since $0.7 > 0.3$). More generally, given two fuzzy problems $\mathcal{F}\mathtt{pb}$ and $\mathcal{F}\mathtt{pb}'$, the degree with which $\mathcal{F}\mathtt{pb}'$ fulfills the conditions of $\mathcal{F}\mathtt{pb}$ is denoted by $\mathcal{F}_{\Leftarrow}(\mathcal{F}\mathtt{pb}, \mathcal{F}\mathtt{pb}')$. For example, $\mathcal{F}_{\Leftarrow}(\mathcal{F}\mathtt{srce}_1, \text{Fernande}) = 0.3$. Moreover, it is assumed that $\mathtt{pb} \Leftarrow \mathtt{pb}'$ iff $\mathcal{F}_{\Leftarrow}(\mathtt{pb}, \mathtt{pb}') = 1$.

This management of fuzzy thresholds has been implemented in the first version of KASIMIR, in an object-based formalism (see [18] for the algorithm of fuzzy hierarchical classification, and [8] for knowledge representation details). For the OWL DL version of KASIMIR, this raises the issue of fuzzy description logics (see, e.g., [24]). More precisely, what is needed here is a description logic inference engine managing fuzzy concrete domains [25]. For both systems, $\mathcal{F}_{\Leftarrow}$ is implemented thanks to the computation of the degree of subsumption between two concepts.

4.5 Managing multiple viewpoints in CBR

The example of Marcelle (Sect. 3.3) points out that the patients may be viewed differently according to the treatment categories (surgery, etc.). Let $\mathtt{s}$:Marcelle and $\mathtt{c}$:Marcelle be the representation of Marcelle according respectively to surgery and chemotherapy. This means that $\mathtt{s}$:Marcelle (resp., $\mathtt{c}$:Marcelle) is a projection of the representation of Marcelle according to the features relevant to surgery (resp., to chemotherapy). In particular, the size of the tumor (S_{tumor}, expressed in centimeters) is kept in both $\mathtt{s}$:Marcelle and $\mathtt{c}$:Marcelle, whereas the size of the breast (S_{breast}, whose domain is $\{\mathtt{small}, \mathtt{standard}, \mathtt{large}\}$) is present in $\mathtt{s}$:Marcelle but not in $\mathtt{c}$:Marcelle. $\mathtt{s}$ and $\mathtt{c}$ are two *viewpoints*, i.e. two subsets of the problem and solution attributes (for the sake of simplicity, only two viewpoints are considered in this section). A problem $\mathtt{pb}$ considered in a viewpoint $\mathtt{v} \in \{\mathtt{s}, \mathtt{c}\}$ is the projection $\mathtt{v}{:}\mathtt{pb}$ of $\mathtt{pb}$ on the set of attributes $\mathtt{v}$. A solution $\mathtt{Sol}(\mathtt{v}{:}\mathtt{pb})$ of $\mathtt{v}{:}\mathtt{pb}$ is a surgical recommendation if $\mathtt{v} = \mathtt{s}$ and a chemotherapy recommendation if $\mathtt{v} = \mathtt{c}$. The protocol itself can be split into viewpoints. In particular, the part of the protocol on surgery recommendation consists in the source cases $(\mathtt{s}{:}\mathtt{srce}, \mathtt{Sol}(\mathtt{s}{:}\mathtt{srce}))$.

The patient Marcelle is considered as a standard patient from a chemotherapy viewpoint: there exists a source case $(\mathtt{srce}_1, \mathtt{Sol}(\mathtt{srce}_1))$ such that $\mathtt{c}{:}\mathtt{srce}_1 \Leftarrow \mathtt{c}$:Marcelle. Thus, the chemotherapy recommended for Marcelle is $\mathtt{Sol}(\mathtt{c}{:}\mathtt{srce}_1)$. By contrast, $\mathtt{s}$:Marcelle is out of the protocol: the feature S_{tumor} is different from the standard. The adaptation consists in introducing a virtual patient $\mathtt{s}$:Marceline with $S_{\text{breast}} = \mathtt{standard}$ and with the same rate between tumor size and breast size as for $\mathtt{s}$:Marcelle, which involves a feature $S_{\text{tumor}} = 5$ cm for $\mathtt{s}$:Marceline. This virtual patient $\mathtt{s}$:Marceline is standard: there exists a source case $(\mathtt{srce}_2, \mathtt{Sol}(\mathtt{srce}_2))$ such that $\mathtt{s}{:}\mathtt{srce}_2 \Leftarrow \mathtt{s}$:Marceline. The recommended surgery for Marcelle is therefore $\mathtt{Sol}(\mathtt{s}{:}\mathtt{srce}_2) =$ radical mastectomy. This example illustrates how a patient can be considered differently and leads to different adaptations according to different viewpoints (like a patient with a large tumor in surgery and with a small tumor in chemotherapy). Moreover, it applies a particular form of case combination: two different source problems are reused to solve a single target problem (for Marcelle, the recommendation is the set of decisions $\{\mathtt{Sol}(\mathtt{c}{:}\mathtt{srce}_1), \mathtt{Sol}(\mathtt{s}{:}\mathtt{srce}_2)\}$).

In this example, the viewpoints are considered as independent one from the others. In practice, there may be bridges between viewpoints relating a feature in a viewpoint with a feature in another viewpoint. This CBR approach, based on multiple viewpoints, is called *decentralized* CBR and is detailed in [11], with a complex example in breast cancer treatment. In [11], the knowledge representation formalism is C-OWL (*Context OWL* [26]), initially designed for reasoning with several ontologies and based on *distributed description logics* [27].

4.6 Integration

In Sects. 4.1 to 4.5, various aspects of protocol adaptation have been modeled in a CBR process involving retrieval, adaptation and combination steps of CBR. These aspects have been considered independently one from the others. The integration issue is "How could these aspects be integrated in a sole CBR architecture?" This section presents how integration is planned, based on the following scenario: the user inputs the description of a target patient $\mathtt{tgt}$ and the KASIMIR CBR system outputs a set of solutions $\mathtt{Sol}(\mathtt{tgt})$ of $\mathtt{tgt}$, associated with explanations (in the form of adaptation paths, that constitute traces of the reasoning steps leading to $\mathtt{Sol}(\mathtt{tgt})$) and ranked with a preference ordering.

In fact, two issues addressed above deal with the integration of heterogeneous aspects of adaptation: the first handled by similarity and adaptation paths (Sect. 4.1) and the second handled by decentralized CBR (Sect. 4.5). The first deals with the combination of heterogeneous adaptation steps, each of them relying on a reformulation. The second deals with different viewpoints, realizing different adaptations in parallel, leading to a complex solution $\mathtt{Sol}(\mathtt{tgt})$ composed of the solutions $\mathtt{Sol}(\mathtt{v}{:}\mathtt{tgt})$, for each viewpoint $\mathtt{v}$. These two approaches are integrated as follows. First, the target problem is projected on each viewpoint $\mathtt{v}$ in a problem $\mathtt{v}{:}\mathtt{tgt}$. The bridges from a viewpoint $\mathtt{v}$ to another viewpoint $\mathtt{v}'$ are used to infer information about the problem $\mathtt{v}'{:}\mathtt{tgt}$ from the problem $\mathtt{v}{:}\mathtt{tgt}$. Then, each $\mathtt{v}{:}\mathtt{tgt}$ is solved independently, by a CBR process local to $\mathtt{v}$, on the basis of similarity and adaptation paths, and of reformulations $(\mathtt{v}{:}\mathtt{r}, \mathcal{A}_{\mathtt{v}:\mathtt{r}})$ defined in the viewpoint $\mathtt{v}$. A CBR process in the viewpoint $\mathtt{v}$ then leads to a solution $\mathtt{Sol}(\mathtt{v}{:}\mathtt{tgt})$ of $\mathtt{v}{:}\mathtt{tgt}$. Finally, bridges from $\mathtt{v}$ to $\mathtt{v}'$ enable to infer new information on $\mathtt{Sol}(\mathtt{v}'{:}\mathtt{tgt})$ from $\mathtt{Sol}(\mathtt{v}{:}\mathtt{tgt})$.

In order to integrate the three other issues in this framework, reformulations $(\mathtt{r}, \mathcal{A}_{\mathtt{r}})$ representing these kinds of adaptations are introduced. The reformulation encoding the adaptation of Sect. 4.2 is simply $(\Rightarrow, \mathcal{A}_{\Rightarrow})$ (the choice between several possible adaptations according to the Wald pessimistic criterion is linked with the ranking of solutions, presented at the end of the section). The adaptation patterns for case-based decision support that are mentioned in Sect. 4.3 can be operationalized in reformulations, using additional domain-dependent knowledge. Therefore, this adaptation approach can be integrated in the adaptation paths.

The use of fuzzy thresholds (Sect. 4.4) can also be integrated in the adaptation paths in the form of a reformulation. Indeed, let us consider the protocol with some replacement of crisp thresholds with fuzzy ones: source cases $(\mathtt{srce}, \mathtt{Sol}(\mathtt{srce}))$ are replaced with $(\mathcal{F}\mathtt{srce}, \mathtt{Sol}(\mathtt{srce}))$, where $\mathcal{F}\mathtt{srce}$ is obtained by replacing in $\mathtt{srce}$ 0, 1, or several crisp threshold(s) with fuzzy threshold(s) (for 0, $\mathcal{F}\mathtt{srce} = \mathtt{srce}$: the classical set of patients represented by $\mathtt{srce}$ can be considered as a fuzzy set of patients). Now, let $\lessapprox$ be the binary relation between two fuzzy problems defined by $\mathcal{F}\mathtt{pb} \lessapprox \mathcal{F}\mathtt{pb}'$ if $\mathcal{F}_{\Leftarrow}(\mathcal{F}\mathtt{pb}, \mathcal{F}\mathtt{pb}') > 0$ (meaning that $\mathcal{F}\mathtt{pb}'$ fulfills the conditions of $\mathcal{F}\mathtt{pb}$ with a non-null degree). With $\mathcal{A}_{\lessapprox} = \mathcal{A}_{\Leftarrow}$, this leads to define the reformulation $(\lessapprox, \mathcal{A}_{\lessapprox})$, that encodes the following adaptation rule:

if $\mathcal{F}\mathtt{pb}$ is fulfilled with a certain degree by $\mathcal{F}\mathtt{pb}'$
then $\mathtt{Sol}(\mathtt{pb}') = \mathtt{Sol}(\mathtt{pb})$ is a solution of $\mathtt{pb}'$

which is a way to represent a kind of fuzzy reasoning.

Now, the question remains of how the results of these reasoning processes—the solutions $\mathtt{Sol}(\mathtt{tgt})$ associated with adaptation paths—can be ranked. Except for the reformulation $(\Rightarrow, \mathcal{A}_{\Rightarrow})$, the costs associated with the reformulations can be used to compute the length of a similarity path, and the solutions are ranked according to a decreasing value of this length. For the reformulation $(\lessapprox, \mathcal{A}_{\lessapprox})$, $\mathtt{cost}(\mathtt{pb} \lessapprox \mathtt{pb}')$ is a decreasing function of $\mathcal{F}_{\Leftarrow}(\mathtt{pb}, \mathtt{pb}')$. In the example of Sect. 4.4, this means that $\mathtt{cost}(\mathcal{F}\mathtt{srce}_1 \lessapprox \mathtt{tgt}) > \mathtt{cost}(\mathcal{F}\mathtt{srce}_2 \lessapprox \mathtt{tgt})$, inducing a preference for the source case $(\mathcal{F}\mathtt{srce}_2, \mathtt{Sol}(\mathtt{srce}_2))$. Note that $(\Leftarrow, \mathcal{A}_{\Leftarrow})$ is a particular case of $(\lessapprox, \mathcal{A}_{\lessapprox})$, which corresponds to a low cost: if $\mathtt{pb} \Leftarrow \mathtt{pb}'$, then $\mathcal{F}_{\Leftarrow}(\mathtt{pb}, \mathtt{pb}') = 1$, and thus, $\mathtt{cost}(\mathtt{pb} \Leftarrow \mathtt{pb}')$ is minimal.

For ranking two adaptations performed by $(\Rightarrow, \mathcal{A}_{\Rightarrow})$ the cost function is insufficient: $\mathtt{cost}(\mathtt{pb} \Rightarrow \mathtt{pb}')$ is a function involving problems, not the solution $\mathtt{Sol}(\mathtt{pb})$ whose consequences have to be examined. This is where the Wald pessimistic criterion can be used. For example, let us consider again the case of Julie and the two similarity paths (1) and (2) (Sect. 4.1). If $\mathtt{cost}(\mathtt{pb} \Rightarrow \mathtt{pb}')$ depends only on $\Rightarrow$, then the lengths of these two similarity paths are equal. This is only after adaptation that the two solutions $\mathtt{Sol}_{(a)}(\mathtt{tgt})$ and $\mathtt{Sol}_{(b)}(\mathtt{tgt})$ obtained by following the adaptation paths corresponding respectively to the similarity paths (1) and (2), can be compared, and this comparison may be based on the worst possible consequences of these decisions, i.e., according to the Wald pessimistic criterion.

Finally, the use of the semantic Web recommendations of the W3C for the development of KASIMIR is helpful for the purpose of integration. Indeed, these standards have been designed to facilitate the interoperability in a knowledge-based system.

This complex model of protocol adaptation requires some knowledge. The problem of acquiring this knowledge is presented hereafter.

5 Adaptation knowledge acquisition for KASIMIR

Adaptation knowledge acquisition (AKA) aims at providing adaptation knowledge for a CBR system. This section gives an overview on the AKA approaches for the KASIMIR system.

5.1 AKA from experts

The AKA from experts approach consists in studying adaptation operations carried on by oncologists. Details on AKA from experts and the lessons learnt are given in [23]. This study shows in particular that the notion of adaptation path is helpful to decompose a complex adaptation process in a sequence of simpler adaptation steps: for having a better understanding of the adaptation operations performed by the experts, and for pointing out the "simple" protocol adaptations that are generalizable.

This AKA has led to the general models for protocol adaptation presented in Sect. 4. To be operational, these models need to be instantiated thanks to specific knowledge, that has the form of adaptation rules, and that is extracted with the help of the CABAMAKA system.

5.2 CABAMAKA: AKA based on knowledge discovery

CABAMAKA is a system dedicated to case base mining for AKA [28]. It reuses the main ideas of the AKA system presented in [29] and the principles and techniques of knowledge discovery from databases (KDD [30]).

An adaptation process following the transformational approach to analogy [31] may be modeled as follows. Firstly, a representation $\Delta\mathtt{pb}$ of the variations from $\mathtt{srce}$ to $\mathtt{tgt}$ is computed. Secondly, adaptation knowledge is used for computing $\Delta\mathtt{sol}$ (variations on problems) from $\Delta\mathtt{pb}$. Finally, $\Delta\mathtt{sol}$ is applied on $\mathtt{Sol}(\mathtt{srce})$ to compute $\mathtt{Sol}(\mathtt{tgt})$.

According to this model, the adaptation knowledge is the knowledge useful for the computation $\Delta\texttt{pb} \mapsto \Delta\texttt{sol}$. CABAMAKA—and the system presented in [29]—learns this knowledge from the variations within the case base: the training set is the set of pairs $(\Delta\texttt{pb}_{ij}, \Delta\texttt{sol}_{ij})$ where $\Delta\texttt{pb}_{ij}$ represents the variations between two source problems $\texttt{srce}_i$ and $\texttt{srce}_j$ and $\Delta\texttt{sol}_{ij}$, the variations between $\texttt{Sol}(\texttt{srce}_i)$ and $\texttt{Sol}(\texttt{srce}_j)$.

The learning process in CABAMAKA uses a powerful data-mining technique, namely the algorithm CHARM [32], implemented in the platform CORON that is developed in the Orpailleur team [33]. The KDD process is interactive: an analyst guides the process before and after the mining step, in particular, for filtering and controlling the knowledge extraction, and then for interpretation and validation.

5.3 Ongoing researches on AKA

The current version of CABAMAKA shows two main limitations. The first is related with the huge amount of results given by the data-mining process, making explorations and interpretations difficult. More precisely, the extracted information units are frequently closed itemsets, each of them likely to be interpreted as an adaptation rule. A current direction of research aims at organizing these itemsets, in order to simplify their navigation. This can be done by introducing quality measures on itemsets (as it is done, e.g., for association rules [34]), or by designing a hierarchy or a lattice.

The second limitation of CABAMAKA lies in the difficulty of associating an explanation to an adaptation rule. It is very costly and perhaps not conceivable to ask an analyst (a domain expert) to associate and/or validate such an explanation to every extracted adaptation rule.

A future work is to understand how the CABAMAKA system could help the analyst in the validation and explanation of adaptation rules, based on adaptation patterns (cf. Sect. 4.3). The idea is that a candidate adaptation rule extracted by the data-mining process could instantiate an adaptation pattern and thus, could inherit its explanation. The role of the analyst would be only to validate/invalidate an explanation, and not to write one from scratch.

A third research idea for AKA is knowledge extraction from texts holding on breast therapeutic decision meetings. Indeed, for several months, these texts have been collected in a semi-structured computer form with plain text fields, that may be exploitable.

6 Implementations

The different parts of the KASIMIR system presented are at different degrees of achievement (from the ones that are operational to the ones that are only planned). This section details this point.

The application of protocols is operational in both versions of KASIMIR (the object-based version and the semantic portal based on OWL DL). Moreover, the object-based KASIMIR system is accessible and used on the Web for several protocols dedicated to oncology (http://www.hermes.asso.fr/KasimirWeb).

Hereafter, the roles of the KASIMIR CBR system are made precise, and then, the implementation states of the protocol adaptation are discussed:

- The KASIMIR CBR system can be used to test the modeling of protocol adaptation;
- It can be used as a case-based decision support system for assisting the decision making processes by proposing argumented decisions (e.g., during breast therapeutic decision meetings);
- Its development involves the definition of a language for expressing adaptation cases, that are medical cases consisting in three parts: the problem `tgt`, the solution `Sol(tgt)`, and the representation of the reasoning operations leading from `tgt` to `Sol(tgt)` (the adaptation path), associated with explanations.

The CBR module of the semantic portal using reformulations, similarity paths, and adaptation paths, is implemented, but is not yet used in the healthcare environment. This implementation is described in [35].

The study about the use of the Wald pessimistic criterion for case-based decision support is, at the moment, purely theoretical.

The adaptation patterns for case-based decision support are not implemented yet, but some of the reformulations that instantiate them have been represented in the CBR module of the semantic portal.

The fuzzy thresholds have been implemented and tested in the object-based version of KASIMIR [8, 18]: the object-based knowledge representation formalism developed for KASIMIR has been extended by introducing fuzzy intervals (i.e., fuzzy sets of integers or real numbers defined by trapezoidal functions). As mentioned above, for the KASIMIR semantic portal, what is needed is an inference engine for a fuzzy description logic, i.e., a description logic where concepts (resp., roles) are interpreted as fuzzy subsets (resp., fuzzy relations) of the interpretation domain. These formalisms have been theoretically investigated these last years and, more recently, work on the development of inference engines for fuzzy description logics has been realized (see [25, 36, 37]). There are multiple ways of introducing fuzziness in a classical description logic. A way of interest is to introduce fuzziness at the level of concrete domains, in particular, for the definition of concepts based on numerical constraints, such as the concept of patients with an age a satisfying the fuzzy condition $\mu_{\leq 40\pm 5}(a)$.

Implementation of multiple viewpoint reasoning and decentralized CBR depends on the development of a reasoner within C-OWL. Such a reasoner exists and is called DRAGO [38], but it does not for the moment support all the features necessary for KASIMIR (in particular, the reasoning on instances). Nevertheless, tests have been carried out within the KASIMIR system on the current version of this reasoner, and they give the expected results.

Finally, the CABAMAKA system is currently working and gives interesting results. The system has been implemented in a modular way, and the dependency on the representation of cases has been reduced to the minimum. Thus, the reuse for another CBR application should not require significant development efforts.

7 Related work in medical CBR

In medical CBR systems, adaptation has often a key role to play, as argued in [39], in which several kinds of adaptations are presented. One of them is constituted by "adaptation operators or rules", that confront the issue of a knowledge acquisition bottleneck. Besides, the need of explanations in medicine is crucial: without them, the solutions provided by a CBR process are hardly accepted by physicians [40]. That is why explanations have to be attached to the solutions suggested by the KASIMIR system. For adaptations, explanations take the form of adaptation paths (describing the reasoning process), with an explanation associated with each step of the path. Several other issues that should be addressed by a CBR system in health science are outlined in [41] and in [42]. Among them is the need to keep the case base up to date, since medicine is a rapidly changing field and guidelines are regularly updated. This issue, which has not been addressed in KASIMIR yet, constitutes a future research work. In fact, since the KASIMIR case base is the protocol, this issue meets the issue of protocol evolution. Another promising research issue is to take advantage of the Semantic Web technologies to achieve interoperability among CBR systems, and to provide a common vocabulary to describe and to share cases and medical ontologies on the Web. This issue is investigated in the Mémoire project [43], where a framework for the exchange of biomedical cases and ontologies using OWL as representation language is proposed. KASIMIR also contributes to this issue since medical protocols are formalized in OWL (more precisely, in the subset OWL DL of OWL), and an OWL vocabulary for reformulations is proposed in [44].

This work shares some features with other studies in medical CBR. For example, the system CARE-PARTNER applies CBR in the domain of stem-cell transplant [45]. This system relies on rules, generalized cases (called *pathways*), and specific cases. Rules and pathways are applied and customized to the target problem, whereas specific cases are adapted. By contrast, in KASIMIR, all the cases can be considered as prototypical: they describe clinical diagnostic categories in terms of symptoms for which a particular therapeutic decision is prescribed by the medical protocol. General cases are adapted (currently, the KASIMIR system does not manage specific cases). These cases are acquired by modeling the protocol. Indeed, a protocol is originally a non formal document, destinated to the physicians, including a lot of implicit knowledge. Thus, case base acquisition and representation involve the modeling and representation of a medical protocol, with the help of experts. Another approach followed by [46] is to acquire prototypical cases from the medical literature.

8 Conclusion and future work

This paper has presented a general picture of research on CBR within the KASIMIR project. More precisely, it studies the adaptation processes of a medical protocol for breast cancer treatment, for patients for which the protocol cannot be applied in a satisfactory manner. Starting from practical examples, this study has led to several issues for case-based decision support, in particular for case retrieval, case adaptation, and case combination.

The first issue is that adaptations may be complex, because there are several reasons to adapt the protocol. This issue has been addressed by introducing the notions of similarity path, adaptation path, and reformulation. The second issue is that information units that are relevant to decision making may be missing for a particular patient. This issue has been addressed through the Wald pessimistic criterion, expressing that a decision should be taken on the basis of its worst possible consequences. The third issue stands that case-based decision support can be performed by the study of the applicability, the expected consequences, and the negative consequences of a decision. Adaptation patterns have been designed for this purpose. The fourth issue is linked with decision thresholds in the protocol: for a value close to a threshold, the decision could be associated with values below or above the threshold. This issue is addressed by replacing crisp thresholds with fuzzy thresholds, that can be represented in fuzzy description logics where fuzziness is introduced at the level of concrete domains. The fifth issue is linked with the different viewpoints of the decision makers: a person in charge of a surgery decision considers a different set of features on the patient from the one of a person in charge of another medical specialty. This issue is addressed by decentralized CBR, i.e., CBR with multiple viewpoints, and to a formalism of distributed description logic.

Finally, the integration of these issues in a CBR system has been studied.

The present research topics can be reused for other applications of CBR, in particular, medical applications and decision support applications. Indeed, the approaches of CBR described here are rather general and domain-independent, though they require some knowledge acquisition work (from experts or semi-automatic) to be fully operational: they belong to knowledge-intensive approaches to CBR. This is why the most important current work in the KASIMIR project is on adaptation knowledge acquisition.

The ongoing work aims at making operational modules that are not yet operational, for an integration in the healthcare environment. This requires ergonomical work: important efforts have to be done on user interface, to make the interaction of KASIMIR with physicians as practical as possible. Moreover, a careful study on the human environments in which introducing KASIMIR future components has also to be done.

The theoretical and practical investigation about protocol evolution, based on frequently performed adaptations, is another future work of the project. This requires (and thus motivates) the representation of adaptations performed by the experts, which is one of the results on the researches on protocol adaptation.

Moreover, it is *not* assumed that all the issues raised above cover all the situations of protocol adaptation. For example, (rather rare) adaptations performed during breast therapeutic decision meetings consisted in changing the order between the treatment components. Working with adaptation involving temporal representation in the therapeutic decision may be another future direction of work.

Another future work may consist in the use of specific cases, in addition with generalized cases. These specific cases can be extracted from medical records which would require, in particular, an anonymization process.

Finally, as presented in Sect. 2, beyond application and adaptation of the protocol, there is protocol evolution, which has to be studied in accordance with the models of protocol adaptation: an adaptation may be seen as a temporary change of the protocol, for a particular patient. An evolution, by contrast, may be seen as a long-term change of the protocol, from frequently performed adaptations.

Acknowledgements KASIMIR is a long term project, involving, with the authors of this paper, a number of persons that we want to thank for their advices and support. In particular, there are physicians (special thanks to Pierre Bey, Isabelle Klein, Ivan Krakowski, Maria Rios, and Danièle Sommelet), developers (for the most important developments, Sébastien Brachais, Benoît Bresson, Julien Cojan, Olivier Croissant, Jérôme Haquin, Sandrine Lafrogne, Julien Lévèque, and Fabien Palomarès), and specialists in psycho-ergonomics (Pierre Falzon, Vanina Mollo, and Catherine Sauvagnac). We thank also the many other persons involved in discussions, tests, etc. And last, but not least, the authors wish to thank the reviewers for their comments.

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