

Modeling of Clinical Practice Guidelines for Interactive Assistance in Diagnostic Processes

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Abstract—Clinical Practice Guidelines (CPGs) include recommendations for actions and therefore provide a frame of reference for the medical practitioner during diagnostic processes. To facilitate the implementation of this recommendations we propose an interactive assistance. For this reason the CPGs of Chronic Myeloid Leukemia (CML) and Myelodysplastic Syndromes (MDS) are modeled using UML activities and Bayesian networks. To lower the barriers of CPG implementation we establish an interface between experts and models. It is based on translation rules transferring UML activities to Bayesian networks. The resulting models are used to provide an innovative assistance function allowing intuitive deviations from given CPG recommendations.

Keywords: Clinical Practice Guidelines, Diagnosis, Interactive Assistance

1. Introduction

A challenge of the medical diagnostic today can be seen in the reviewing and evaluation of the huge amount of publications. For example: A search of the term “myelodysplastic syndrome diagnosis” in Pubmed [1] yields about 12000 results. For a decision maker a profound inquiry concerning a specific topic can therefore be extremely laborious. Moreover, the steady growth of published findings makes it almost impossible for an individual to keep their knowledge up-to-date [2].

With the use of Clinical Practice Guidelines (CPGs) the consolidated medical knowledge can be condensed into general recommendations of actions. High quality CPGs are proposed by bodies of experts with respect to the current state of research [3]. Consequently, for an individual medical practitioner, CPGs open up a scope of actions and decisions in the context of a contemporary diagnostic practice.

In addition to the development and dissemination of a CPG (see Figure 1) the actual implementation of recommendations by the medical partitioner plays a decisive role. The physician has to adapt a diagnostic algorithm to the given boundary conditions (patient, equipment, medical experience) [4], [5]. Consequently there is a gap between theoretical knowledge and practical solutions. Additionally, barriers can arise from (for example) low acceptance of CPGs on the part of the physician. The described situation is subject of many researches [6], [7], [8], [9].

A passive dissemination (e.g. distribution via print media) has only little effect on the actual practitioners behavior [4]

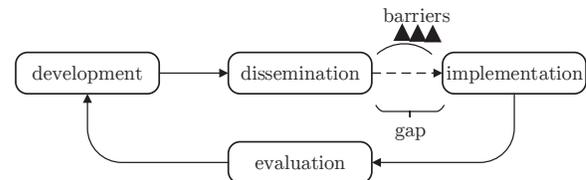


Fig. 1: Stages of a Clinical Practice Guide (CPG). The recommendations are development and disseminated. There is a gap between theoretical knowledge and practical actions performed by the medical practitioner. Additionally there can be barriers that have to be overcome.

[5]. Therefore we propose an interactive assistance of the practitioner during the diagnostic process which helps to reduce the gap between theoretical knowledge and practical solutions and helps to overcome barriers.

Barriers can arise from different CPG stages [10]. We are convinced that most of them could be moderated by creating the possibility to modify the recommendations by the practitioner himself. This includes for example the reduction of fear of regimentation or short-term modifications due to medical symposia etc. That’s why our approach of modeling medical knowledge comprises a dialogue between technical and medical domain experts as well as the modification of knowledge by the medical expert himself.

2. Approach of Modeling CPGs

Usually CPGs contain knowledge in form of texts and schematic diagrams that can not automatically be translated into models without further ado. We believe that the formalization of knowledge can be done via an expert dialog (see Figure 2). Therefor experts from the medical- and from the technical domain are necessary. Together they develop a CPG model in the form of a UML activity. Alternatively, the guideline can be interpreted by the medical expert, only. This approach is useful if a practitioner wants to modify an already existing UML activity independently. This bypass could help to lower barriers during the CPG implementation.

The benefit of our approach is that it is based on a UML activity. Different models representing the CPG can automatically be generated by only one given activity. Therefor, we developed translation rules. The UML activity in Figure 2 serves as an interface for the actual models used for providing assistance functions. These functions propose suitable examination values to the practitioner during the diagnostic process.

The automatic translation of a UML activity into a Petri net is based on the work of Störrle et. al [11], [12]. A

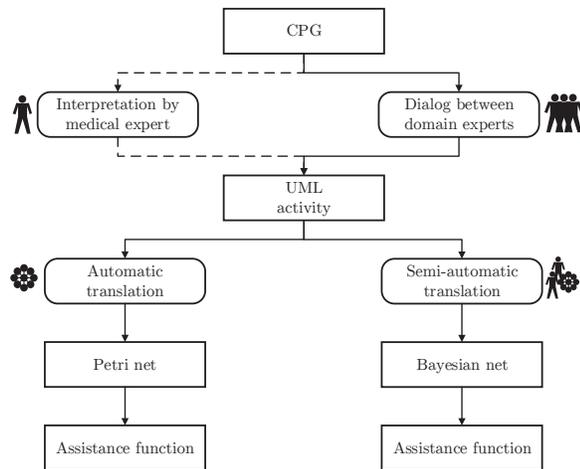


Fig. 2: A CPG is transformed into a UML activity by an expert's dialog. A bypass of the procedure is introduced to allow an exclusive modification by the medical expert. The UML activity serves as an interface to the models used for providing the actual assistance functions. These models are (semi-) automatically generated from the UML activity by translation rules.

new approach is used to semi-automatically translate a UML activity into a Bayesian net. What makes this translation semi-automatic is the fact that the parameters of the net (i.e. conditional probabilities) have to be assessed manually once the net structure is automatically generated from the activity. In this paper we focus on the translation of UML activities into Bayesian nets.

3. Construction of the Interface

UML activities have been chosen as an interface because their syntax is formalized and analyzed by various experts [13]. Furthermore, UML is accepted in software industry worldwide [13], [14], [15]. A huge benefit of UML activities is their easy comprehensibility for the medical- as well as the technical domain experts. This is a necessary precondition to make the experts' dialog work smoothly and to allow modifications by the medical expert on his own.

3.1 State of the Art

The UML 2.4 comprises a total of 14 different chart types which can be divided into structural and behavioral diagrams [14]. Activity diagrams are among the latter and thus model not the static but the dynamic behavior of a system and its components. Thus, an activity answers the question of how a particular process or algorithm proceeds [14]. Control flows, object flows, actions, decisions and forks can be used to specify such an activity [15].

Figure 3 shows the typical routings which appear in the guideline models Chronic Myeloid Leukemia (CML) and Myelodysplastic Syndromes (MDS). The black dot represents the start of an activity (initial node), whereas the double circle corresponds to the end of an activity (activity final). The rounded rectangles are the actions that are to be performed, while the arrows represent the flow. Subfigure a) shows a case where actions are carried out one after another (sequential). Subfigure b) depicts a selective routing. Only

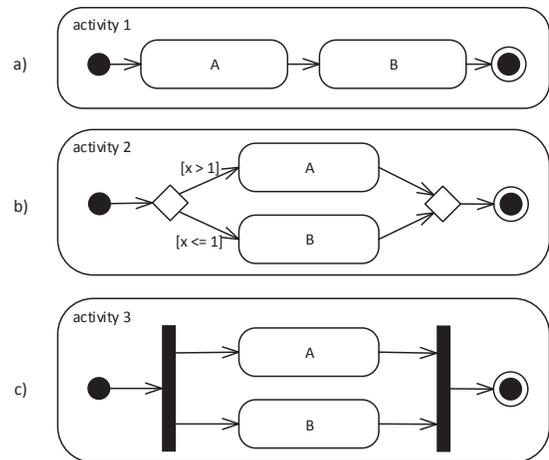


Fig. 3: The subfigures show the 3 typical routings appearing in the CPG models of CML and MDS. In a) the actions A and B are sequentially performed (one after another). In b) there is a decision to be made in order to perform either A or B. c) shows a routing where A and B are performed concurrently. Consequently both actions are performed in any possible order.

one of the two actions A and B is performed. The decision is represented by a diamond (decision node) and depends in this example on a variable x which is either greater 1 or not. The second diamond is called merge node as it merges the two possible flows. Subfigure c) shows a case where two actions can be performed concurrently. The flow is split up by a so called fork node (black bar). The join node on the right synchronizes the flows. As a consequence the flow continues, i.e. the activity ends, only iff both actions have been performed (in any arbitrary order).

3.2 Modeling of a Particular Disease

Figure 4 shows the UML activity for CML. Due to the complexity of the CML CPG and the resulting size of the corresponding UML activity, the sketch emphasizes some parts of interest (magnifying glasses).

Subfigure a) depicts a sequence of actions. The first action is "suspicion of CML". That's an important precondition, since there are different CPGs for different diseases. Consequently the diagnosis algorithms of a CPG normally start with a specific suspicion for the disease under consideration. The second action is anamnesis (case history). During the anamnesis the practitioner asks the patient if he feels bone pain, i.e., the value "bone pain" is a result of the activity "anamnesis". We used a so called pin notation to specify a value as an output parameter for a given action [16]. The third action "physical examination" generates the output "spleen size". Actions can have several output- or input parameters.

Subfigure b) shows the action "Verify CML". This action involves some kind of assessment. Namely, the practitioner has to decide whether or not the examination values are proofing the disease. Therefore the decision if a disease is present is not modeled in a deterministic way (i.e. not by fixed rules). The final decision is up to the medical expert.

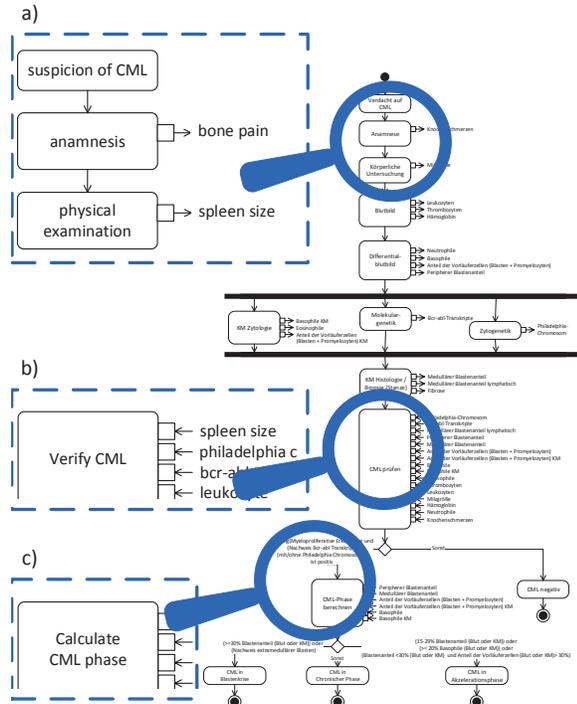


Fig. 4: In the background of this figure the UML activity for CML is shown. Because of the size of the activity the sketch emphasizes some parts of interest (magnifying glasses). Subfigure a) shows a sequential order of actions. Subfigures b) and c) show two different types of actions. The first one is a decision based on examination values that cannot be made by deterministic rules. Consequently the medical expert has to decide what to do - not the model. The second action is a decision which is based on a fixed rule (e.g. thresholds for particular blood test results).

Another decision is shown in Subfigure c). The keyword “calculate” emphasizes that this decision can be made on the basis of a specific rule. In this example, which type of CML is present can be derived by evaluating fixed rules (e.g. thresholds for particular blood test results).

The activity for MDS is about twice the size of the CML activity. The MDS activity is not shown in this paper, since the basic underlying concepts are the same as for CML. However, one important difference between the two diseases CML and MDS exists: In case of CML the practitioner is searching for examination values (e.g. blood test values) that proof the presence of the disease. MDS in contrast is a diagnosis of exclusion, i.e. rather than proofing MDS, known differential diagnoses of MDS are excluded. If all of the differential diagnoses are excluded, it is assumed to be proven that MDS is present¹.

4. Bayesian Nets

Medicine is a famous area of application for Bayesian networks [17]. They are well suited for diagnostic processes because the probability for a diagnosis can be calculated by

¹This modus operandi is known from quizshows like “Who Wants to Be a Millionaire?” – i.e. by excluding 3 of possible 4 answers the candidate is able to deduce the right answer.

successively adding examination values. Using this approach the practitioner can complete fragmentary examination values independent of a fixed sequence of tests.

4.1 State of the Art

Bayesian networks are probabilistic graphical models (PGMs) since they combine graph theoretic approaches with approaches of probability theory. They can be used to represent a probability distribution more compactly by taking advantage of independencies between variables. For the representation of these independencies the representation as a graph seems to be natural.

A Bayesian network consists of a probability distribution P and a graph $G = (V, E)$, whose vertex set V represents the set of random variables $U = \{X_1 \dots X_n\}$. Directed edges between two nodes $V_i \rightarrow V_j$ represent a direct dependency between two variables - a missing edge represents the independence of these two variables. The graph to the underlying network is both directed and acyclic, this is abbreviated as DAG [18], [19], [20].

4.2 Transformation of a UML Activity

Given a UML activity represented as a graph $U =$ (activity nodes, activity edges). The set of activity nodes be further divided into sets of nodes:

- \mathcal{A} : Set of actions,
- \mathcal{S}, \mathcal{E} : Initial node and final node,
- \mathcal{B} : Set of decision- and merge nodes (branch nodes),
- \mathcal{C} : Set of fork- and join nodes (concurrency nodes),
- \mathcal{O} : Set of object nodes.

The set of object nodes is given by the set of data pins. A node that is part of one of the node sets $\mathcal{S}, \mathcal{E}, \mathcal{B}, \mathcal{C}$ is called a control node. Furthermore, the set of activity edges is given by

- \mathcal{KF} : Control flow, i.e. activity edges between actions and control nodes as well as between them underneath each other.
- \mathcal{DF} : Object flow, i.e. activity edges between actions and object nodes or between control nodes and object nodes.

Formally, the translation $[[U]]$ of a UML activity U to a DAG $G = (V, E)$ of a Bayesian network is given by:

$$[[(\text{activity nodes, activity edges})]] = (V, E),$$

where:

$$V = \{e_j \mid (e_i, e_j) \in \mathcal{DF}, e_i \in \mathcal{O}, e_j \in \mathcal{A}\} \tag{1}$$

$$\cup \{e_i \mid (e_i, e_j) \in \mathcal{DF}, e_i \in \mathcal{O}, e_j \in \mathcal{A}\} \tag{2}$$

$$\cup \{v \mid v \in \mathcal{A}, \text{Depth}(v) = 1\} \tag{3}$$

$$E = \{(e_j, e_i) \mid (e_i, e_j) \in \mathcal{DF}, e_i \in \mathcal{O}, e_j \in \mathcal{A} : e_j.\text{contains}(\text{“verify”})\} \tag{4}$$

$$\cup \{(e_i, e_j) \mid (e_i, e_j) \in \mathcal{DF}, e_i \in \mathcal{O}, e_j \in \mathcal{A} : e_j.\text{contains}(\text{“calculate”})\} \tag{5}$$

$$\cup \{(e_i, v) \mid v \in \mathcal{A} : \text{Depth}(v) = 1, e_i \in \mathcal{A} : e_i.\text{contains}(\text{“verify”})\}. \tag{6}$$

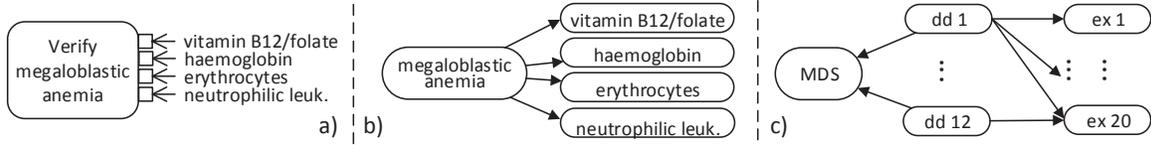


Fig. 5: Subfigures a) and b) depict the translation of a UML action. Node and pins are transformed to vertices in the Bayesian net. There are directed edges from diagnosis to examination values since diseases cause specific test results. Subfigure c) shows the Bayesian structure for a diagnosis of exclusion like MDS.

It is assumed that the nodes of the Bayesian network have a unique name. If a UML activity diagram has several activity nodes with the same name (e.g. as pins of different actions), it is indeed translated several times. But since the destination node has the same name in each case, it is added to the Bayesian network only once. That's because adding an element to a set where the element is already part of, does not alter the set.

UML actions that are provided with input pins representing either a diagnosis, a score or a phase of a disease. Actions are transformed to vertices of the corresponding Bayesian net (1). The pins of these actions are transformed to vertices as well (2). They are providing examination values for an action which can be a non-deterministic verification (diagnosis) or a deterministic calculation (score or phase of a disease due to thresholds etc.).

Since diseases cause typical test results, there is a directed edge from diagnosis to the relevant examination values (4). This is a causal interpretation of an edge². The process of translation is depicted in Subfigures 5a) and 5b). In case of a deterministic calculation the direction of an edge is reversed (5). That is because the examination values are causing a specific score or phase.

The distinction of the cases (4) and (5) are not given by the activity's structure. But the translation can be performed by searching for a specific keyword in the action's name. The function contains checks if a keyword is present. The keyword "verify" represents a non-deterministic verification and "calculate" represents a deterministic calculation.

The translation rules (3) and (6) apply for a diagnosis of exclusion like MDS. In this case we get a special network structure where all differential diagnosis become parents of the diagnosis of exclusion (see Subfigure 5c)).

4.3 Network Structure and Parameters

The network structure for a disease like CML follows Subfigure 5b). For an diagnosis of exclusion like MDS, the application of translation rules generate a Bayesian network structure outlined in Subfigure 5c). The conditional probability table (CPT) of MDS is given by

$$P(MDS|D_1, \dots, D_{12}) = \begin{cases} 1, & \text{if } MDS = f(D_1, \dots, D_{12}) \\ 0, & \text{otherwise} \end{cases}$$

$$\text{where: } f(D_1, \dots, D_{12}) = \neg D_1 \wedge \dots \wedge \neg D_{12}. \quad (7)$$

²A Bayesian net reflecting the causal structure normally reflects the expert's understanding of a domain and is therefore useful if the parameters of a net are to be assessed by a survey.

Because many differential diagnosis have an impact on several examination values, the corresponding examination nodes can have several parent nodes. For example the examination node haemoglobin has 10 parents. Even if all these involved random variables are binary, this would lead to a haemoglobin CPT with 2^{10+1} values (half of them, i.e. 2^{10} have to be explicitly specified). To build all the CPTs in a robust fashion, we reduced the large amount of values by using some simplifications. We used noisy ORs [21] to reduce the number of parameters for binary nodes with n parents from 2^n to $2n$. Consequently the number of parameters increases linearly with the number of parents. For random variables with more than 2 states the so called noisy MAX model was used to reduce the number of parameters [21], [22], [23]. Due to the lack of a patient database, the network structure was parametrized by the results of a survey. A medical expert was asked to answer 90 questions concerning the MDS diagnostic and to answer 60 questions concerning the CML diagnostic.

4.4 Assistance Function

In the models of CML and MDS, the diagnostic node plays a key role. It represents the probability distribution over the states of the disease under consideration. The question is, which evidence can be set to make one of the variable's states as much likely as possible? Regarding a practitioner this means: Which examination value leads to a situation where the decision maker can tell most certain whether the disease is present or not. Consequently, examination values are taken that reduce uncertainty.

A measure of the uncertainty of a random variable is the entropy [24]. It is the higher the more the probability mass scatters over the states of the random variable. In case of a uniform distribution the entropy is maximum. With regard to the diagnostic node that means that the more likely the variable takes one of the 2 states "present" or "not present", the lower the entropy is. Therefore, the reduction of entropy is an essential part of the assistance function.

Let A be a discrete random variable with n states a_1, \dots, a_n and $P(A)$ the probability distribution. Then the entropy η (in bits) is given by [24]:

$$H(A) = - \sum_{i=1}^n P(a_i) \log_2 P(a_i), \quad (8)$$

$$\text{where: } H(A) \in [0, \log_2(n)].$$

The graph of the entropy for a random variable with 2 states can be described by a concave function. The function reaches its maximum value of $\log_2(2) = 1$ if both states of

the random variable are equally likely. If one of the 2 states has a probability of 0 the entropy drops to 0, too. In this case we removed the uncertainty about the state of the random variable.

The entropy of a random variable A (e.g. diagnosis) given a random variable B (e.g. examination value) is given by the conditional entropy [24]:

$$H(A|B) = H(A) - I(A, B). \quad (9)$$

$I(A, B)$ is called the mutual information and represents the reduction in the uncertainty of A due to the knowledge of B.

Thus, the benefit of an examination E_1 can be rated by its effect on the uncertainty of a random variable D that represents the (non-)presence of a disease. Hence, formula (9) may be rearranged to give:

$$I(D, E_1) = H(D) - H(D|E_1). \quad (10)$$

If there are several possible examinations E_i that can be performed, we would prefer the one with the highest mutual information (i.e. highest reduction of uncertainty about D). Thus, a preliminary assistance function recommending an optimal examination E^* can be obtained:

$$E^* = \arg \max_{E_i} (H(D) - H(D|E_i)). \quad (11)$$

Given a Bayesian net with a node representing the random variable D, the entropy $H(D)$ can be calculated by formula (8). The conditional entropy $H(D|E_i)$ is defined as [24]:

$$H(D|E_i) := \sum_{j=1}^n P(E_i = e_j) H(D|E_i = e_j), \quad (12)$$

where $j=1 \dots n$ are states of random variable E_i .

The conditioned entropy $H(D|E_i = e_j)$ in equation (12) is the entropy of the variable D given a certain value e_j of E_i . Thus, $H(D|E_i)$ is calculated by averaging $H(D|E_i = e_j)$ over all possible values e_j that E_i may take.

In a real medical scenario, the choice of an optimal examination solely on basis of equation (11) is not feasible. This would mean that an examination that is very specific for a disease would be suggested first (high benefit), regardless of whether this examination is highly invasive or costly which might outweigh its diagnostic benefit.

The order of the examinations listed in the recommendations of the CPG is a result of the consideration of different interests (costs). Among other things, the invasiveness of an examination is considered. At the beginning of the diagnosis process the proposed examinations are less invasive than at the end of the diagnostic process when the practitioner is more convinced a disease is present or not.

We propose a weighted reduction of uncertainty for integrating cost-benefit considerations during the diagnosis process into our assistance function. The decision maker has the opportunity to choose to what extent to follow the CPG recommendations or to consider a higher reduction of

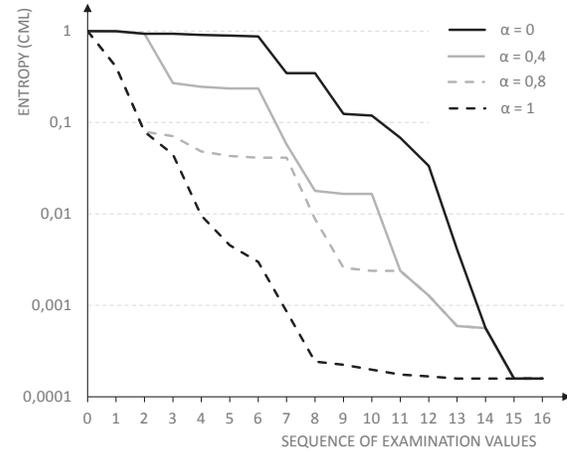


Fig. 6: Entropy of the node CML versus the order of executed examinations. The first examination value obtained is assigned with sequence number 1. Tables 1 lists the assignment of the examination values to the numbers used in the diagram for $\alpha = 0$. By following the CPG recommendations, the entropy decreases slowly at the beginning of the diagnostic process (solid black line).

uncertainty during the diagnostic process:

$$\text{Recommendation}_i = (1 - \alpha)(1 - k_i/m) + \alpha I(D, E_i),$$

where k_i : depth of examination E_i in CPG ,
 m : overall depth of CPG ,
 α : weight factor .

To allow cost-benefit considerations, the assistance function can be adjusted by the parameter alpha. For $\alpha = 1$ only the reduction of uncertainty is taken into account (benefit). Respectively, for $\alpha = 0$ the recommendation follows exactly the given CPG model (cost). The increase of the parameter alpha allows to specify how much the practitioner wants to deviate from the CPG recommendations in favor of a uncertainty reduction. The reduction of uncertainty seems to be a realistic reason for not following a CPG recommendation in practical work.

5. Verification and Validation

In a first demonstration, the examination values on a patient with suspected CML are assessed in the order given by the corresponding CPG recommendation. The assistance function is therefor parametrized with $\alpha = 0$ and consequently only the costs given by the CPG are considered.

Figure 6 depicts the reduction of entropy for $\alpha = 0$ while observing more examination values (solid dark line). By following the CPG recommendations, the entropy decreases slowly at the beginning. With the 11th examination value the entropy has dropped below 0.1. The highest reduction of uncertainty is observed after late examinations. These examinations are highly invasive but are important for identifying the disease for sure. The examination values of the patient are listed in Table 1.

In a second demonstration, $\alpha = 1$ is chosen. The black dotted line in Figure 6 represents the corresponding progress of the entropy. In this case the assistance function proposes

Table 1: Patient with suspected CML ($\alpha = 0$).

No.	Depth	Examination value	Entropy
0	0	-	1
1	1	Bone pain negative	0,996791632
2	2	Spleen enlarged	0,937185857
3	3	Haemoglobin $< 13g/dL$	0,937185857
4	3	$150k/\mu L \leq$ Thrombocytes $\leq 400k/\mu L$	0,908302337
5	3	$10000/\mu L <$ Leukocytes	0,895383409
6	4	Neutrophilic leukocytes increased	0,873765252
7	4	$1\% \leq$ Basophilic leukocytes $< 20\%$	0,346539286
8	4	Progenitor cells $\leq 30\%$	0,346539286
9	4	$15\% \leq$ Peripheral blasts $< 30\%$	0,124546345
10	5	Progenitor cells bone marrow $\leq 30\%$	0,119056765
11	5	$20\% \leq$ Basophilic leukocytes bone marrow	0,068089434
12	5	$5\% <$ Eosinophilic leukocytes	0,033581937
13	5	Philadelphia chromosome positive	0,004083213
14	5	Bcr-abl positive	0,000563717
15	6	$15\% \leq$ Medullary blasts $< 30\%$	0,000158269
16	6	Lymphatic progenitor cell positive	0,000158269

examinations that maximize the reduction of uncertainty in each step. Highly risky and invasive examinations are recommended first, because they are able to reduce uncertainty the most.

Instead of considering either cost ($\alpha = 0$) or benefit ($\alpha = 1$), our assistance function can be parametrized with $\alpha \in (0, 1)$. This allows cost-benefit considerations. For $\alpha = 0.4$ (solid gray line in Figure 6) the very first examinations (anamnesis, physical examination) are done as the CPG is suggesting. The entropy drops with examination 3. In this examination it is tested whether the so-called Philadelphia chromosome is present or not. The Philadelphia chromosome is a strong indicator for CML [25]. As a result there is an earlier reduction of uncertainty in the diagnostic process.

Figure 7 shows a plot of MDS entropy against the number of a differential diagnosis. The initial value of the entropy is moderately at around 0.5. This is due to the fact that a certain a-priori probability is assigned to each of the 12 differential diagnoses of MDS which influences the probability distribution of MDS. Firstly, the state "present" of MDS is unlikely, even though there is the suspicion of MDS. Medically, this seems plausible and was confirmed by the expert's setting of the corresponding a-priori probabilities of the differential diagnoses: Despite of the suspicion of MDS, first, the more likely differential diagnoses have to be excluded. The more differential diagnoses are excluded, the more likely MDS is present. MDS is present for sure, once all differential diagnoses have been excluded.

The progression of the entropy in Figure 7 reflects this fact. Initially MDS is unlikely, so the plot does not start with the maximum entropy. By successively excluding the differential diagnoses, the entropy first increases to a value close to the maximum of 1. Here $MDS = positive$ and $MDS = negative$ are about equally likely. As more and more excluded differential diagnoses make a positive diagnosis of MDS likely, the entropy falls. The individual entropy values for $\alpha = 0$ is shown in Table 2.

Given is now a patient whose diagnosis has already been established. Patient data suggests that molecular genetics

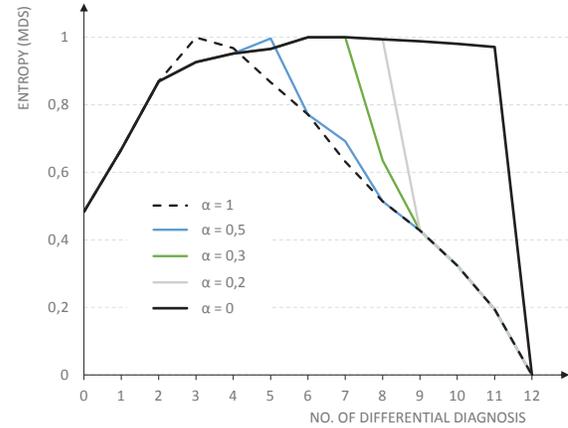


Fig. 7: Entropy of the node MDS versus the order of excluded differential diagnoses for different values of α . If all differential diagnoses are excluded, MDS is present for sure - the entropy drops to 0.

Table 2: Patient with suspected MDS ($\alpha = 0$).

No.	Depth	Examination	Entropy
0	0	-	0,483273525
1	1	Megaloblastic anemias negative	0,667357598
2	1	Reactive bone marrow alterations negative	0,869280269
3	1	Toxic bone marrow damage negative	0,926423147
4	2	Monocytosis of other etiology negative	0,951739499
5	3	Hypersplenism negative	0,965406878
6	4	Immune thrombocytopenia negative	0,999630334
7	4	Paroxysmal nocturnal hemoglobinuria negative	0,999958433
8	5	Acute leukemias negative	0,993451440
9	6	Congenital dyserythropoietic anemias negative	0,987947563
10	7	Hairy cell leukemia negative	0,980510718
11	7	Aplastic anemia negative	0,970950594
12	7	Myeloproliferative diseases negative	0

and bone marrow histology were actually carried out earlier during the process of diagnosis than is recommended by the guideline. The reproduction of this case in the model yields to a situation in which according to the CPG 4 differential diagnoses still have to be excluded. These are "congenital dyserythropoietic anemia", "hairy cell leukemia", "aplastic anemia" and "myeloproliferative neoplasms" (see Figure 8). The assistance function proposes to exclude "congenital dyserythropoietic anemia" next, since the guideline suggests to do so ($\alpha = 0$). By setting an alpha value of 0.3, it appears clear that the exclusion of myeloproliferative neoplasia in terms of the cost-benefit ratio is better than the exclusion of congenital dyserythropoietic anemia. This is exactly what happened in the real world: the practitioner recognized the higher probability of a "myeloproliferative neoplasia" because of his expertise, and decided to exclude this particular disease by molecular genetics and bone marrow histology.

To sum up, it can be said that the models for CML and MDS behave as expected. They are able to describe the corresponding diagnostic process and can provide the intended assistance function. Real world cases can be reproduced with appropriate alpha values. The parameter alpha ranges somewhere in between 0 and 1 (avoiding the extreme values 0 and 1) since medical cases are based on the consideration

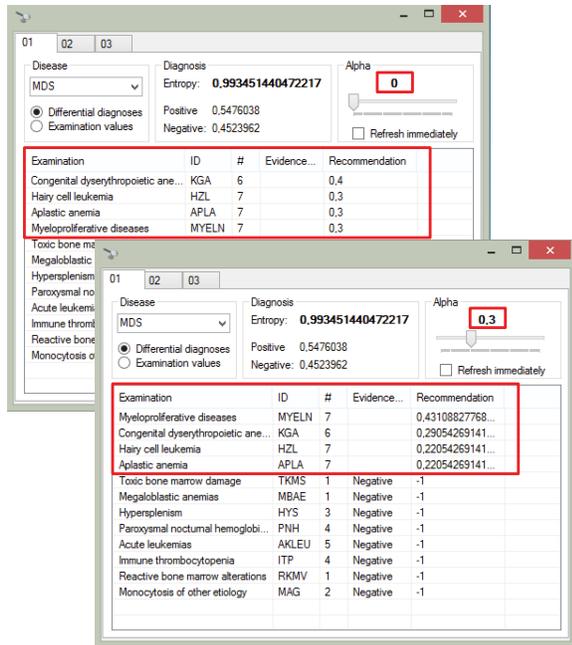


Fig. 8: User interface of the assistance function. There are 4 differential diagnoses left.

of the CPG recommendations as well as the reduction of uncertainty about the presence of a disease.

6. Conclusion

In this paper we introduced the concept of an interface between experts and CPG models used for supporting the practitioner during the diagnostic process. Our approach utilizes UML activities as a basis for a CPG formalization done by a medical and/or technical expert. An activity can then be translated into different CPG models such as Petri nets or Bayesian nets. These models are used to provide the actual assistance function. In this work we focused on the transformation of UML activities into Bayesian networks.

The assistance function provided by a Bayesian net is based on the reduction of uncertainty and the sequence of recommended examinations given by a CPG. During the diagnostic process it provides the practitioner with recommendations which next examination value to take. In contrast to assistance functions based on rigid CPG models, our assistance function allows to weigh up costs and benefits of a certain examination. To which degree the reduction of uncertainty outweighs the costs (e.g. due to invasiveness of an examination) can be adapted individually.

For the future, we plan to take our approach to the next level by integrating it in a real world diagnostic application that helps to overcome barriers in CPG implementation and reduces the gap between theoretical medical knowledge and practical solutions.

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