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Ontology-Based Approach for Liver Cancer Diagnosis and Treatment

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Abstract
Liver cancer is the third deadliest cancer in the world. It characterizes a malignant tumor that develops through liver cells. The hepatocellular carcinoma (HCC) is one of these tumors. Hepatic primary cancer is the leading cause of cancer deaths. This article deals with the diagnostic process of liver cancers. In order to analyze a large mass of medical data, ontologies are effective; they are efficient to improve medical image analysis used to detect different tumors and other liver lesions. We are interested in the HCC. Hence, the main purpose of this paper is to offer a new ontology-based approach modeling HCC tumors by focusing on two major aspects: the first focuses on tumor detection in medical imaging, and the second focuses on its staging by applying different classification systems. We implemented our approach in Java using Jena API. Also, we developed a prototype OntHCC by the use of semantic aspects and reasoning rules to validate our work. To show the efficiency of our work, we tested the proposed approach on real datasets. The obtained results have showed a reliable system with high accuracies of recall (76%), precision (85%), and F-measure (80%).

Keywords HCC · Ontology · Medical image · Classification systems · Web Ontology Language (OWL)

Introduction

Liver tumors characterize hepatic masses, malignant or benignant, localized inside liver tissue. These diseases could damage liver cells especially in advanced stages. HCC is one of the most dangerous and malignant liver tumors. According to the CDC (US Centers for Disease Control and Prevention) statistics, each year in the USA, about 22,000 men and 8000 women get liver cancer, and about 16,000 men and 8000 women die from hepatic diseases. Among the symptoms, we

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find jaundice, weight loss, and fatigue. In our work, we concentrate in this type of cancer by applying semantic aspects.

Ontology presents a shareable and a common structure of information between human and machines; it removes terms ambiguities and allows the reuse of domain knowledge. It is defined originally as an explicit formal specification of the terms in the domain and relations among them [1]. It has been included in different fields such as semantic web, biology, and medicine for instance. This popularity is due to its ability to reduce problem complexity. The present paper concentrates on the medical domain and the use of ontology as a computational aid for clinical problems. In fact, medical ontologies are included to treat problems related to medical and biomedical domains such as diagnosis and disease treatment. The literature shows a variety of approaches describing the most famous medical ontologies [2–7].

This diversity of medical projects reveals the importance of using ontology in this domain. Besides, the purpose of medical image analysis is extracting information automatically from one image or from a sequence of images in order to assist the diagnosis process or the physician's intervention. Nowadays, different modes of image acquisition, such as computed tomography (CT) and magnetic resonance imaging (MRI), are used in clinical routine. Several works were done such as [8–11]. However, these works were based on low-level image characteristics such as color, texture, and shape without taking into consideration reasoning offered by semantic representation. Also, in the domain of liver cancer, especially HCC disease, there exist only a few works that introduce ontology for liver tumor detection, a reason encouraging us to develop a new ontology-based approach especially for HCC diagnosis. In this way, the objective is to develop a Java prototype in order to assist radiologists in the diagnostic process. This work describes methods allowing HCC detection and classification. It gives an overview about related works. Also, it presents our proposed approach by explaining the functional architecture and the programming languages used.

HCC Detection and Staging

Radiologists use medical image (e.g., MRI) usually to detect several diseases. In the case of HCC, this detection starts when a hepatic nodule was observed in the image. The parameters that evaluate the existence of HCC are the size of the nodule, its vascular profile, the level of the alpha fetoprotein (AFP), and the characteristics of signals T1 and T2 allied to the MRI sequence.

Diagnosis of HCC often requires using diagnostic algorithms such as LI-RADS (Liver Imaging Reporting and Data System) and cancer classification and staging systems such as BCLC (Barcelona Clinic Liver Cancer), TNM (Tumor, Node, and Metastasis), GRETCH ("GRoupe d'Etude et de Traitement du Carcinoma Hépatocellulaire"), JIS (Japan Integrated Staging), CLIP (Cancer of Liver Italian Program), CUPI (Chinese University Pronostic Index), and Simplified staging [12]. In this paper, we are interested in the LI-RADS, BCLC, and TNM systems, which are widely used in clinical practice.

LI-RADS is a standardized system based on terminology and diagnostic criteria. It was approved by the American College of Radiology (ACR). The first release was in 2011. Two revisions have been realized to this system in 2014 and 2017. This system is used to represent, interpret, and report liver imaging tests for patients with cirrhosis or for patients that could be affected by HCC. It takes into account various criteria to determine liver tumor state (i.e., diameter of the detected mass and arterial phase state). This system is also applied to eliminate errors of interpretation [13]. The last update generates seven categories of liver lesions: LR-NC, LR-1, LR-2, LR-3, LR-M, LR-TR, and LR-TIV. Li-RADS is used also to guide radiologists and doctors via standardized liver observations. It generates groups of classification based on the benignity and malignity's probabilities of HCC tumors. Furthermore, it performs the interpretation of medical images such as MRI and CT. Thus, it involves the categorization of each hepatic observation (i.e., hepatic mass observed in the medical image). It can be applied with an algorithm intended for diagnosis [14].

The BCLC staging is considered as the most common classification system for hepatic diseases. It looks for integrating liver functions and tumor characteristics to offer the lesion stage. Also, it focuses on linking each stage with the suitable treatment. It is based on a set of criteria, especially size and extent of the primary tumor, hepatic nodule number, functional index, Child-Pugh score depending on five factors (encephalopathy, ascites, total bilirubin, albumen, and prothrombin), portal vein pressure, and bilirubin level [15, 16]. This score contains three separate stages (A, B, and C). Patients are subsequently assigned to five different stages (0, A, B, C, and D) based on these criteria. The notable functionality that characterizes the BCLC system, compared to other available systems, is the assignment of treatment recommendations for HCC stages based on the best treatment methods currently used. Indeed, BCLC system defines a corresponding treatment for each stage, ranging from curative treatments such as resection or liver transplantation for early-stage patients to symptomatic treatment for end-stage patients. BCLC staging system has gained widespread popularity since its publishing in 1999. It is currently considered to be the standard system for HCC management by the "American Association for the Study of Liver Disease," the "American Gastroenterology Association," the "European Association for the Study of Liver," and the "European Organization for the Research and Treatment of Cancer" [17]. Furthermore, a number of studies on Italian and American cohorts [18–21] have shown that this staging system provides a better prognosis compared to the other commonly used systems. However, the BCLC classification has some limitations. Firstly, the suitable treatment may not be extracted; this is due to its allied stage which contains a variable number of sequences associated to HCC patients. Secondly, this system does not take into account some sensible effects (i.e., underlying risk factors) which make the staging process difficult. Finally, some treatments declared by this system may not be conventional in real clinical routines [12, 17–21].

The TNM system (see Table 1) is an international staging system devised by Professor Pierre Denoix (France) between the years 1943 and 1952. It was published by the Union for International Cancer Control (UICC). It classifies all cancers types based on tumor characteristics. It is considered as a common language that helps professionals to deal with several cancerous cases. It uses notations to represent these characteristics. This system is composed of three criteria: tumor size (T), the presence or absence of nearby metastasis in lymph nodes (N), and the presence or not of distant metastasis in other parts of the body (M). For each of those criteria, a value must be given. The stage interpretation will be indicated later according to these values. This system was developed by the American Joint Committee on Cancer (AJCC) and the International Union for Cancer Control (UICC) and has been updated several times; the 7th one was in 2010 [22]. The 8th edition has been released in 2016 [23]. It is characterized by a variety of benefits. On one hand, it is efficient to catch the HCC stage for various patient cases [12]. On the other hand, other parameters can be integrated in this system without disturbing the stability of the staging module (i.e., fibrosis score). Despite the efficiency of TNM, it has some drawbacks. It is less efficient than other systems, especially for the advanced HCC cases [17]. Also, it does not provide disease treatments. The next section presents related works, including liver cancer diagnosis by using ontology.

Related Work

Treating the hepatitis diseases via ontology is an interesting topic, which several research works have dealt with. Previous studies have shown that ontology is efficient to surpass different medical gaps. Also, a great deal of effort has been devoted to studying biomedical ontologies. Chan et al. [24] propose an EHR (electronic health record)-based approach, allowing the examination of medical data such as clinical reports. This system is not only dedicated to offer information about patients but also provides a clinical decision support by distinguishing HCC diseases from those reports. It extracts terms related to liver cancer and organizes them by the use of SNOMED (Systematized Nomenclature of Medicine) ontology concepts. In [25], authors present a machine-learning system applying the reference resolution technique. The goal is to automatically extract liver tumor characteristics such as size, number, and cancer stage from textual medical reports. In Oberkampf et al. [26], the authors propose an ontological model called Model for Clinical Information (MCI) based on Open Biomedical Ontologies (OBOs). This model aims to provide semantic representation for medical data extracted from radiological reports. This representation consists of transforming the textual notes into a detailed structural formalization. This approach takes into account these indications to develop a prototype named ReportViewer. Its role is to visualize medical imaging results and classifying them as normal or abnormal. At the same context, Abdel-Badeeh et al. [27] summarize the previous works done by the same authors in the field of integration the knowledge engineering to represent liver cancer diagnosis. Alfonse et al. [28] present a Web-based liver cancer ontology dedicated to interested users and domain experts. In this work, ontology looks at discovering liver cancer location, providing its semantic representation over the Web, and pulling out the stage via TNM classification. The result of this work is an ontological approach shown with its different components: classes, properties, and instances. An Ontology of Biomedical Reality (OBR) system for Viral Hepatitis (VH), including a description of the liver diseases, has been developed by Ibrahim et al. [29]. This framework is offered to both intelligent systems and physicians, which make it easy to share, reason, and exploit this knowledge. The ontological method is described in three main steps: (i) VH ontology extraction phase, (ii) VH ontology validation phase, and (iii) VH ontology representation in Web Ontology Language (OWL) [30] phase. In the same context, AL-Marzoqi et al. [31] develop a novel Web-based approach using ontologies for liver viruses. Indeed, viral hepatitis causes serious complications on the human body. This work enables physicians and students of medicine to differentially diagnose this type of disease. The evaluation part was made by constructing some queries beneficial to retrieve common diseases, symptoms, signs, or laboratory findings from the built ontology. Kokciyan et al. [32] propose a semantic description of liver cancer based on CT scan images. Moreover, this work presents an ontological approach inspired from real radiological reports. This ontology has been available online since 2014 under the name of Ontology of Liver for Radiology (ONLIRA) as a part of the Case Retrieval in Radiology (CaReRa)[1] project [33]. To interpret the proposed approach, the authors gather the most used statements in radiology reports and subsequently make a keyword search. This simulation insists on two major components: a qualitative assessment and a quantitative assessment in order to show the efficiency of ONLIRA. Roldán-García et al. [34] proposed an

[1] http://www.vavlab.ee.boun.edu.tr/pages.php?p=research/CARERA/carera.html

Table 1 TNM staging 8th edition

T, N, M value	Signification	Stage						
		IA	IB	II	IIIA	IIIB	IVA	IVB
T1a	Unique tumor with a size ≤ 2 cm with or without vascular invasion.	✓						
T1b	Unique tumor > 2 cm without vascular invasion		✓					
T2	Unique tumor > 2 cm with vascular invasion or multiple tumors with sizes < 5 cm			✓				
T3	Several tumors with sizes ≤ 5 cm				✓			
T4	Unique or multiple tumor(s) spreading portal hepatic veins and adjacent organs taking into account the diaphragm and other than the gallbladder or with perforation of visceral peritoneum.					✓		
Any T	Any T value						✓	✓
N0	Presence of metastases	✓	✓	✓	✓	✓		
N1	Presence of metastases						✓	
Any N	Any N value							✓
M0	Absence of metastases	✓	✓	✓	✓	✓	✓	
M1	Presence of metastases							✓

ontological approach called Liver Case Ontology (LICO) to model real cases of patients infected by liver diseases. This approach reuses and applies medical terminologies and vocabularies inspired by previous lexical and ontological resources such as International Classification of Diseases, Tenth Revision, Clinical Modification (ICID-10-CM[2]), SNOMED-CT, ONLIRA, RadLex, and the Logical Observation Identifier Names and Codes (LOING[3]). Alfonse et al. [35] propose an ontology-based system for cancer diseases. This work discusses what type of cancer the patient has. This system is based on three basic parts: (i) the diagnostic part which determines the type of cancer, (ii) the staging part using TNM system, and (iii) the treatment recommendation part which subsequently renders the suitable treatment. In AL-Marzoqi et al. [36], the authors investigate the current studies on ontological approaches for hepatobiliary system diseases. This approach concentrates on system organs such as liver, gallbladder, bile duct, and pancreas. It gives an overview of liver-based systems and shows its ontological representation. Parminder et al. [37] describe an ontology-based approach which diagnoses the liver cancer disease. This work presents this type of cancer taking into account risk factors, symptoms, diagnosis process, treatment, investigation of liver cancer, and its prognosis using the TNM classification system. Also, it shows, as evaluation, the taxonomical hierarchy of concepts in liver ontology and its query representation using SPARQL language. Yunzhi et al. [38] exposed an ontological prototype system related to hepatitis disease classification. The proposed system provides a framework for semantic purposes querying and retrieval. It also focuses on searching similarity between terms by applying query expansion. Other works [39, 40] include the medical image of the liver such as MRI or CT scans in the process of diagnosis and present a pure semantic description of the medical context. Table 2 shows a recapitulation of some related works.

Generally, all these works address the problem of liver tumor diagnosis via an ontological approach. They discuss this kind of cancer and suggest different solutions. Quite recently, considerable attention has been paid to detect liver diseases. However, most of the previous studies do not take into account the whole diagnostic process which starts by detecting the hepatic nodule and ends with the suggested treatment. Some works deal with the process of detection module only or deal with the staging module only, and others expose a semantic representation related to liver imaging. In this paper, we present an original ontological approach combining both strategies, i.e., it integrates the medical staging mentioned above (TNM, BCLC) and medical image data in a single framework. Our approach also explores the possibility of extracting the treatment to be applied later.

Thus, our main contributions are as follows:

- Developing an ontology prototype OntHCC that modeling HCC liver cancer. Three major modules should be presented: detection from the medical image, staging the detected nodule, and assisting on the appropriate treatment.
- Ensuring relations and properties that link concepts.
- Integrating reasoning process to query data semantics through the ontology by building Semantic Web Rule Language (SWRL) rules.
- Populating the developed ontology with instances from real patient cases.
- Testing the proposed approach via graphical demonstrators.
- Evaluating OntHCC comparing to other works.

[2] https://www.cdc.gov/nchs/icd/icd10cm.htm
[3] https://loinc.org/

Table 2 Related work summary

Approach	Objectives	Ontology utility	Simulation	Language(s)/tool(s)
LiCO [47]	Modeling LICO, ontology for liver representation, based on known lexicons.	Giving a semantic representation for liver diseases annotation.	Testing with real patient data via reasoning queries.	Protégé SWRL SPARQL OWL
Chan et al., 2017 [24]	HCC liver lesions identification and detection from radiological reports	Retrieving liver cancer terms form clinical reports	Simulation with a database containing 112 abdominal CT imaging	UMLS EHR SNOMED CT
Yim et al., 2016 [25]	Using the reference resolution technique to represent semantically liver cancer tumors	Extracting liver cancer characteristics from textual reports	Recall and precision measures	UMLS MetaMap WordNet
ReportViewer [26]	Using MCI model to classify medical image findings as normal or abnormal	Giving medical interpretation and semantic representation of reported measurements	Uses SPARQL to compare the extracted findings with their real measurement values	SPARQL RECIST
AL-Marzoqi et al., 2015 [36]	Hepatobiliary system diagnosis	Conceptual representation for the hepatobiliary system Giving a new classification method based on the system organs.	Comparison among ontology-based systems for hepatobiliary system diseases	OWL
Parminder et al., 2015 [37]	Ontological approach for liver cancer diagnosis	Giving a semantic representation for liver cancer disease	Using SPARQL to extract information related to liver cancer disease	OWL SPARQL OntoGraph
ONLIRA [32]	Medical image (CT) ontology using RadLex vocabulary.	Semantic description for liver cancer disease	Qualitative/quantitative assessment using semantic/key-words search	Radlex OWL
Alfonse et al., 2014 [35]	Ontological approach for liver cancer disease	Liver cancer diagnosis staging via TNM treatment recommendation	Simulation with a database of cancer ontologies containing three types of cancer	Java OWL-API FaCT++ OWL-DL
Alfonse et al., 2012 [28]	Web-based liver cancer ontology	Discovering liver cancer location providing a semantic representation staging via TNM	Ontological Representation	OWL-DL OWL
Moawad et al., 2012 [29]	OBR framework for Viral Hepatitis (VH)	VH Ontology Design Methodology VH Ontology Extraction Phase(mapping/classifiying between the VH Diseases and their symptoms/signs/laboratory-findings validation phase	VH classification tree	OBR Framework OWL
VHOSWS [31]	A sharable service web bring together doctors and physicians to allow liver cancer diagnosis	Retrieving symptoms/signs/ laboratory findings' hierarchy of viral hepatitis disease	A set of query operations extracting disease specifics	OWL
OntoVIP [39]	OntoVIP framework for medical image annotation	Reusing existing ontologies to realize the semantic representation	Defining a common vocabulary	RadLex vSPARQL
Levy et al., 2009 [40]	Semantic reasoning with image annotations for tumor assessment	Reasoning with the resulting image annotations for tumor lesion assessment	Transforming AIM information into OWL	XML SWRL OWL SQWRL

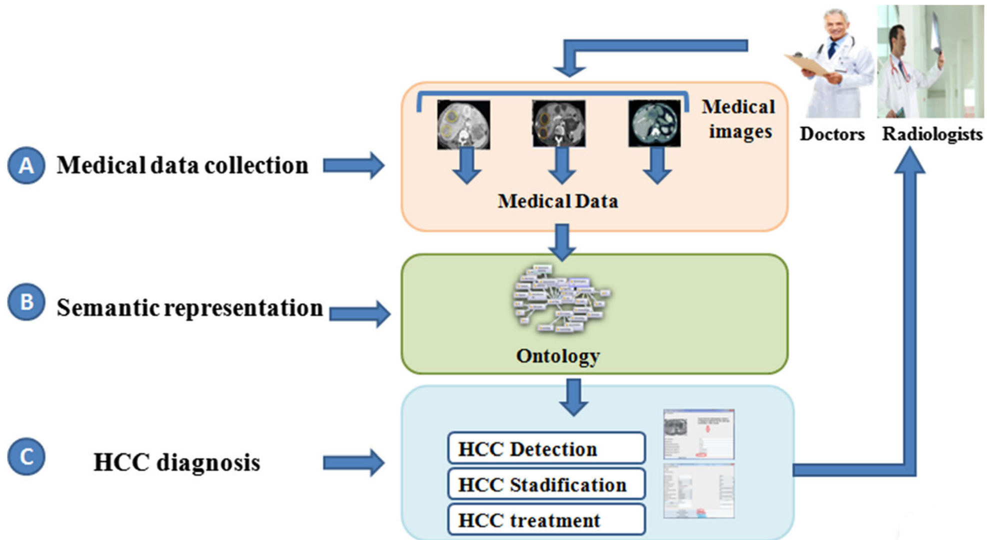

Fig. 1 Ontology-based approach for HCC diagnosis. The proposed approach is composed essentially of three main phases: (A) presents the medical data collection phase, (B) presents the semantic representation phase, and (C) presents the HCC diagnosis phase

Materials and Methods

Data Source

The data used for this article has taken from University Hospital of Clermont-Ferrand (CHU), France. Medical images acquired by doctors, in Digital Imaging and Communications in Medicine (DICOM)[4] format, and other personal data (concerning age, gender, etc.) have been first anonymized and stored in a secured way in servers located in CHU. The patients who have delivered these elements have signed an informed consent, obtained before the procedure. Patients must be able to understand and willing to sign the written informed consent so that medical images and other data can be used for any research issue.

Proposed Approach

Our approach presented in Fig. 1 is composed of three major phases. The first phase focuses on extracting information from medical images. The second makes the semantic description of these images using ontologies. This phase also includes staging systems for liver tumor staging. At this phase, we follow these systems and the SWRL rules [41]. The last phase shows graphical interfaces implemented with Java and having the role of visualizing, HCC detection, functioning of staging systems, and HCC treatment.

Step A: Medical Data Collection

In order to detect HCC from medical images and giving a data model for this disease, we need to focus on some image features. In this section, we present these features. We also present how they lead to specify nodule nature and if it is a HCC or not. This first phase leads to gather information related to the HCC disease tacked from medical imaging, which will be introduced later into the ontology. In the case of medical imaging (MRI, for example), ontology is applied mainly to semantically describe these images and to allow reasoning techniques to diagnose HCC. To detect HCC from MRI, we need to know some information followed frequently by standard classification systems (e.g., BCLC). These information are related to HCC pathology and the tissue cytology such as the nodule size, its vascular profile, the characteristics of the MRI signals, and the alpha-fetoprotein (AFP) level, which is used to help diagnose, monitor the treatment, and check the appearance of cancers. The Child-Pugh score also can be calculated by the use of its five criteria, and its grade will be generated. In this way, distant metastasis can also be detected

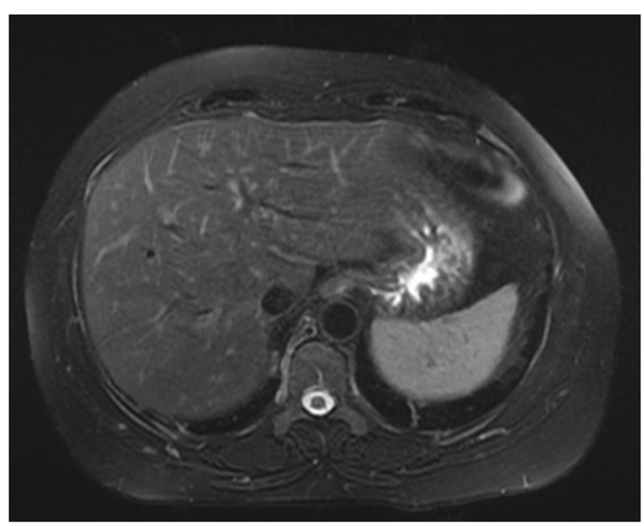

Fig. 2 Liver MRI imaging. This figure illustrates an example of a liver MRI used in the proposed approach

[4] http://www.dicomstandard.org/

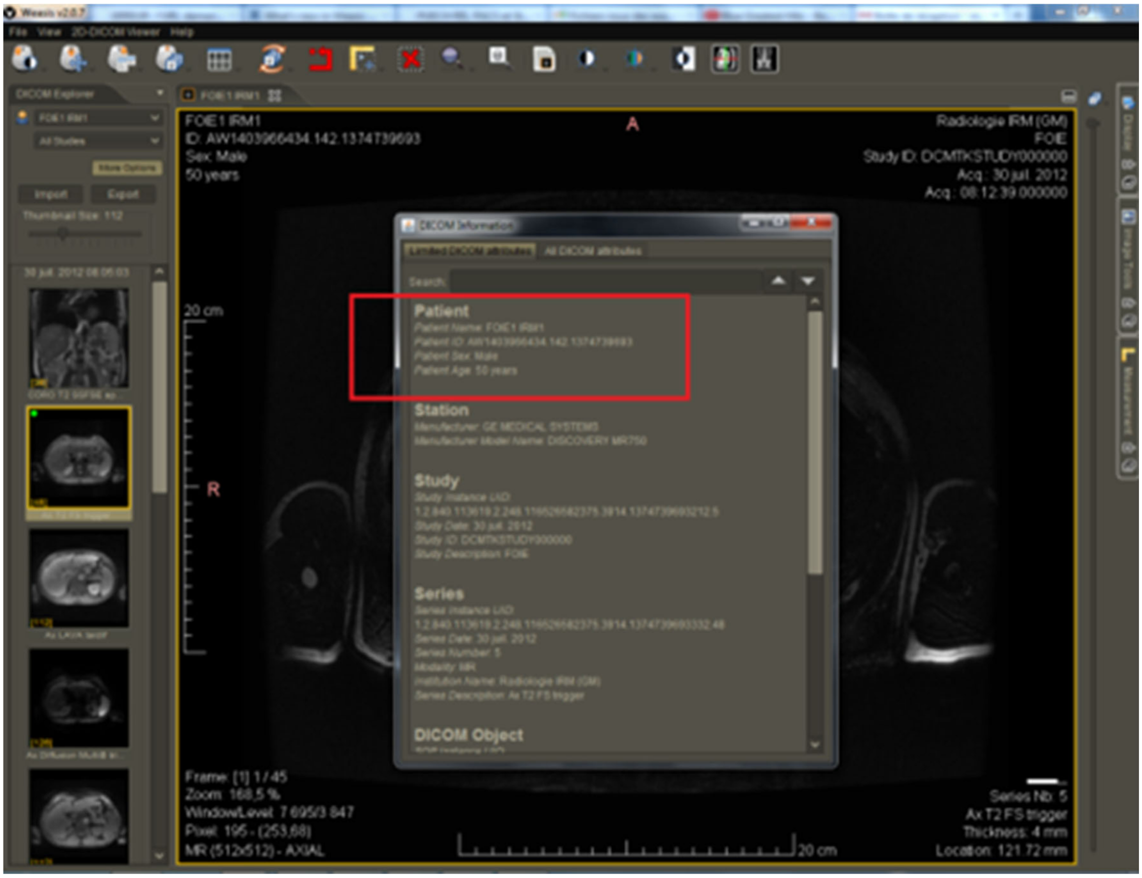

Fig. 3 Extracted data using Weasis. This software is efficient to get information from the DICOM image. Several information related to the infected patient can be extracted such as identifier, name, gender, age, and weight

by the use of liver measure function. Furthermore, to enrich our approach, we use Weasis[5] for DICOM image viewer [42] to read the header of this format and extract information related to the patient. After that, the extracted information will be considered as an entry to the built Ontology: the identifier, name, gender, age, and the weight of the patient. Figures 2 and 3 expose respectively an example of the liver MRI used and its corresponding result using the Weasis software.

Step B: Semantic Representation

During this phase, a detailed semantic description of liver cancer is initiated. We focus on the diagnostic process including symptoms, medical interventions, and risk factors. We reused 12 concepts modeling liver cancer inspired from [28]. These concepts are disease, liver cancer, medical intervention, diagnosis, TNM system, T, N, M, references, symptoms, and risk factors. Also, it models only TNM system stages. We add various other concepts related to BCLC staging, Li-RADS concept to represent the nodule category, medical imaging to interpret its clinical findings, and the hepatic lesion details. Table 3 gives an overview about some OntHCC concepts. In our ontology, we have 49 concepts. They are connected via various object properties. For example, “classifiedInto” is used to link “LiverCancer” and “BCLC-system,” “treatedBy” is used to connect “LiverCancer” and “Treatment,” “hasCategory” links “Nodule” and “LIRADS_Category.” In addition, we include tools to help detecting the HCC from a MRI image such as “Weasis Medical Viewer” which can open easily DICOM images format and visualize the header information and the radiologist interpretation. Our medical ontology was built using Protégé Tool [43] to model HCC image findings and describe liver state. Thus, to ensure a balanced and a coherent ontological model, we chose to follow the methodology MethOntology [44]. Figure 4 shows a part of this ontology via the plug-in OntoGraf [45].

The step of reasoning the ontology through SWRL rules is efficient to make the HCC diagnosis process. Some examples of rules are presented in Table 3. The first rule describes the HCC detection via the medical image, it formalizes the criteria leading to classify the observed nodule as HCC or not. These criteria are as follows: nodule size, the vascular profile which can be “typical” or “atypical,” contrast agent injection, AFP level, and MRI signals T1 and T2 which can be

[5] https://dcm4che.atlassian.net/wiki/spaces/WEA/overview

Table 3 OntHCC concepts and definition

Concept	Definition
Disease	Characterizes the disease type being treated in our work, it is a cancer.
Patient	Presents the individual who undergoing medical examination and following treatment.
MedicalIntervention	Presents medical interventions used by doctors in the diagnoses process (i.e., blood tests)
Diagnosis	Presents the tools used for HCC diagnosis such as MRI and physical exams.
Treatment	Represents the suitable treatment that can be applied later (i.e., surgery, ablation, chemoembolization)
Liver	Presents the liver; it is characterized by various properties (i.e., portal vein pressure, bilirubin level, Child-Pugh score)
Nodule	Characterizes the detected hepatic lesion. It is described by various properties (i.e., number, size)
Stage-TNM	Defines TNM stages. It can be one of these stages IA, IB, II, IIIA, IIIB, IVA, and IVB.
TNM-System	Refers to a staging system that takes as an input several parameters (i.e., tumor size), and it gives as an output stage. It generates seven stages.
T	Refers to the tumor size. The various values are Tout-T, T1, T2, and T3.
N	Refers to the presence or not of metastases in regional lymph nodes.
M	Refers to the presence of metastases in other organs.
References	Presents what follows the doctor or radiologist as mechanisms to diagnose the patient.
Symptoms	Presents HCC symptoms (i.e., loss of appetite, weight loss)
Risk-Factors	Presents the risk factors that increase danger degree for HCC such as alcohol, tobacco, and obesity.
MedicalImage	Represents the image which interprets the doctor to take the medical decision.
BCLC-System	Refers to the BCLC system that we used to stage tumors (i.e., A0, A1, B, C, D)
EarlyStage	Represents the early stage of the BCLC system. It can be A1, A2, A3, or A4.
AdvancedStage	Represents the advanced stage of the BCLC system. It is denoted by C.
UltimateStage	Represents the ultimate stage of the BCLC system. It is denoted by D.
VeryEalyStage	Represents the earliest stage of the BCLC system. It is denoted by A0.
IntermediateStage	Represents the intermediate stage of the BCLC system. It is denoted by B.
TypeLiverCancer	Designs the cancer type. It is an HCC.
HCC	Represents hepatocellular carcinoma. The type of cancer treated in our work.
LIRADS_Category	Represents LI-RADS categories. It used to detect hepatic lesions from medical images and report's findings.
LR_NC	Represents a category of Li-RADS. It characterizes a non categorized lesion because of absence of full information.
LR_1	Represents a category of Li-RADS. It characterizes a benignant lesion.
LR_2	Represents a category of Li-RADS. It characterizes a probably benignant lesion.
LR_3	Represents a category of Li-RADS. It characterizes an intermediate probability of HCC.
LR_M	Represents a category of Li-RADS. It characterizes a non-HCC malignancy.
LR_TR	Represents a category of Li-RADS. It characterizes treatment response algorithm (i.e., nonevaluable, nonviable, equivocal, viable).
LR_TIV	Represents a category of Li-RADS. It characterizes unequivocal enhancing soft-tissue.
Segment	Refers to liver segments. It is composed of seven segments.

"hyperintense" or "hypointense." Rule 2 presents an example of LI-RADS system applied to interpret lesion category. This example takes into account liver and lesion characteristics. Here, "hasDiameter" is a data property corresponding to the lesion. "hasWashout," "hasCapsule," hasEvoluation, and "hasArterialPhase" are data-type properties related to the liver, and "oui," "oui," "non," and "rehaussement-hyper" present respectively their values. They are used to deduct the adequate LI-RADS category which is here "LR_M." The second rule describes the BCLC system classification. The stage tested here is the stage C which is an instance related to the concept "AdvancedStage." The third rule describes the TNM staging system applied in our ontology. In this example; "has-T," "has-N," "has-M," "hasSpreadBloodVessels," "hasSpreadLymphNodes," and "hasSpreadOtherPart" present data-type properties related to the concept liverCancer. "Tout-T," "Tout-n," "M1," "Oui," "Oui," and "Oui" present respectively their values. "Stage-IVB" characterizes an instance of

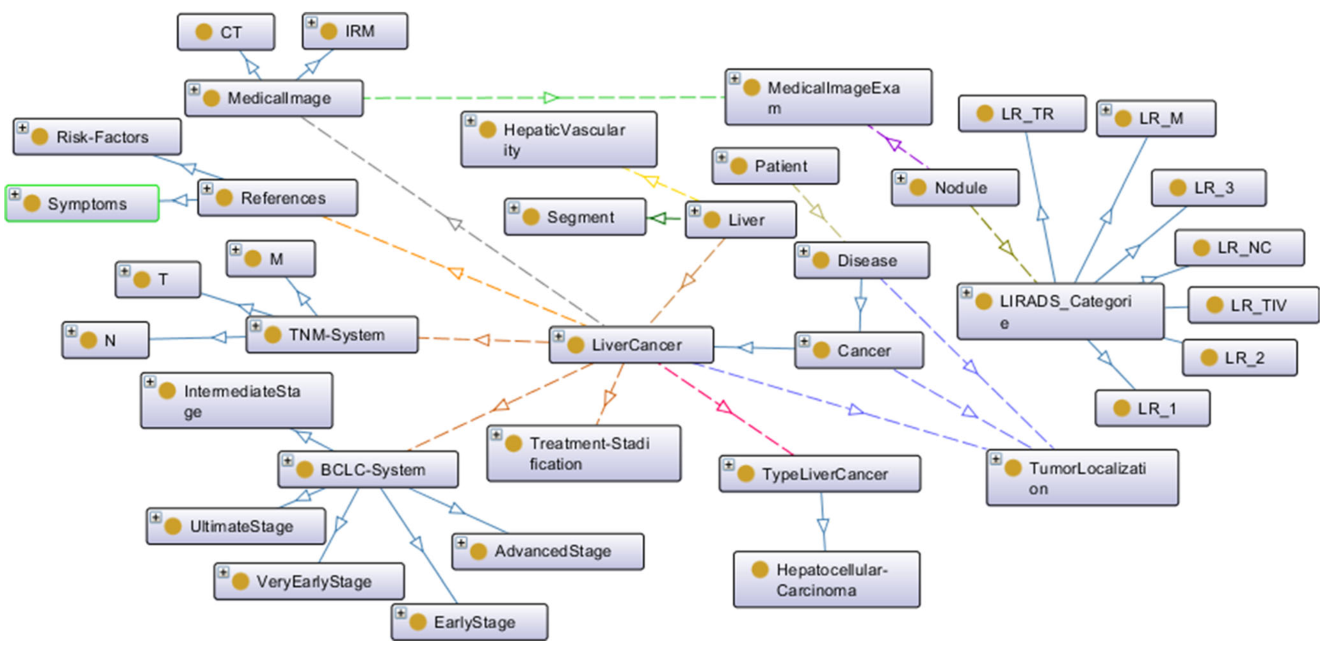

Fig. 4 Visualization of OntHCC prototype via the plugin OntoGraf. The proposed ontology contains 49 concepts; this figure exposes a part of this ontology for modeling liver cancer

the concept "StageTNM." The last rule presents the treatment type which can be applied later to treat the disease. "classifiedInto" is an object property that links "liverCancer" concept to "BCLC-System" concept. "treatedBy" is an object property that links "LiverCancer" concept to "Treatment" concept and A2 is an instance of the concept "EarlyStage."

Step C: HCC Diagnosis

In this step, we include the reasoning offered by ontology to realize the HCC diagnosis. Firstly, we see if the observed nodule refers to a HCC disease or not (detection phase). Secondly, we extract the tumor stage (staging phase). Finally, we try to step out the adequate type of treatment (treatment phase). Figures 5, 6, and 7 respectively expose the developed demonstrators allowing the diagnosis process. Clinicians can use these demonstrators to check out information about MRI images, to extract the nodule stage, and to detect the treatment. This application is based on the developed ontology which will be rich after by the adequate instances.

Implementation

Clinicians need an automatic system which facilitates HCC diagnosis process. To implement our approach, we used different kinds of computing software and programming languages like "Protégé editor" applied to build the medical ontology and to edit Resource Description Framework (RDF) [30] files. Also, "Eclipse IDE" was used to develop the graphical demonstrators. Thus, to achieve communication between both software

Table 4 Examples of SWRL rules

Rule 1:HCC detection	Nodule(?x) ^ MedicalImage(?y) ^ MedicalImageExam(?z) ^ isSequenceOf(?y, ?z) ^ foundIn(?x, ?z) ^ noduleSize(?x, ?s) ^ swrlb:greaterThan(?s, "2") ^ hasVascularProfile(?x, "typical") ^ usesPDC(?z, "Oui") ^ hasAFP(?x, ?a) ^ swrlb:greaterThan(?a, "400") ^ hasSignalT1(?z, "hyperintense") ^ hasSignalT2(?x, "hyperintense") -> hasResultClass(?x, "HCC")
Rule 2:HCC category detection via LI-RADS	MedicalImageExam(?x) ^ Nodule(?y) ^ foundIn(?x, ?y) ^ hasDiameter(?x, "?s") ^ swrlb:lessThan(?s, 20) ^ hasWashout(?x, "oui") ^ hasCapsule(?x, "oui") ^ hasEvoluation(?x, "non") ^ hasArterialPhase(?x, "rehaussement_hyper") -> hasCategory(?y, LR_M)
Rule 3: BCLC system	Liver(?x) ^ LiverCancer(?y) ^ Nodule(?n) ^ composedOf(?y, ?n) ^ noduleSize(?n, ?s) ^ swrlb:greaterThan(?s, 5) ^ noduleNumber(?n, 1) ^ contains(?x, ?y) ^ hasBiluribine(?x, "NonApplicable") ^ hasPortalVeinPressure(?x, "NonApplicable") ^ hasFunctionalIndex(?x, 2) ^ hasScoreChildPugh(?x, "GradeA") -> classifiedInto(?y, C)
Rule 4: TNM system	LiverCancer(?x) ^ has-T(?x, Tout-T) ^ has-N(?x, Tout-n) ^ has-M(?x, M1) ^ hasSpreadBloodVessels(?x, "Oui") ^ hasSpreadLymphNodes(?x, "Oui") ^ hasSpreadOtherPart(?x, "Oui") -> classifiedInto(?x, Stage-IVB)
Rule 5: HCC treatment	LiverCancer(?x) ^ classifiedInto(?x, A2) -> treatedBy(?x, Surgery)

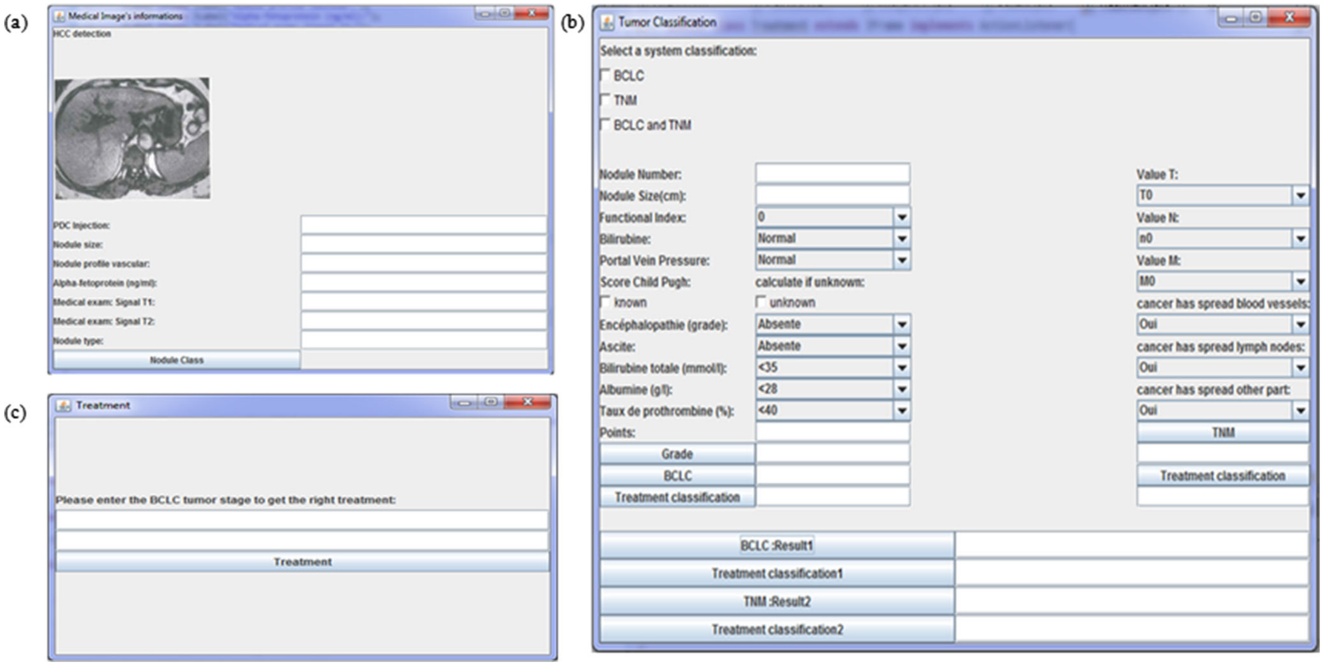

Fig. 5 Ontology-based approach for HCC detection, classification, and treatment. **a** The HCC detection demonstrator allows the extraction of MRI image information and decides if it is a HCC or not. It runs when the user fills in the text fields. This interface is related to SWRL rules modeling HCC detection from MRI imaging (i.e., rule 1 of Table 4). **b** The HCC stadification demonstrator allows the staging of the extracted HCC nodule. Three systems can work at the same demonstrator: BCLC, TNM, and the treatment stadification. This interface is related to SWRL rules modeling essentially BCLC and TNM staging (i.e., rules 2 and 3 of Table 4). **c** The HCC treatment demonstrator allows the determination of the suitable treatment based on the BCLC classification. This interface is related to SWRL rules modeling HCC treatment (i.e., rule 5 of Table 4)

mentioned above, we used "Jena API" [46]. It is a programming toolkit based on the Java programming language and mostly used to create and read RDF files. To extract data from medical images, we used Weasis. Other languages were used to reasoning the ontology such as SWRL language and to query it like Query Language for RDF (SPARQL) [47].

OntHCC: Prototype for HCC Diagnostic Assistance

Our functional architecture contains essentially three main parts as shown in Fig. 8. The expected missions are as follows: medical ontology construction by following MethOntology [44], SWRL rule definition enabling HCC diagnosis, and

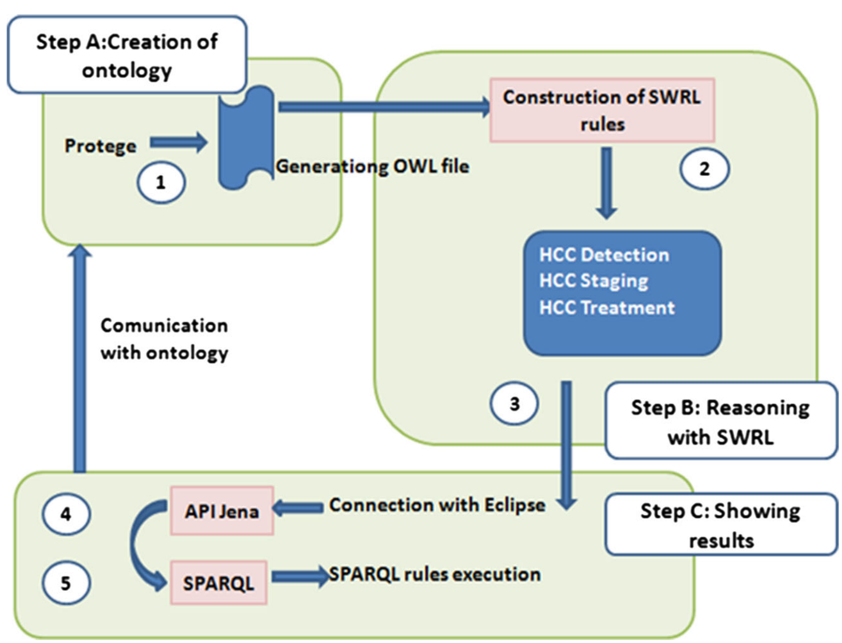

Fig. 6 Functional architecture. The functional architecture applied in this work is composed of three main steps. Step A, creation of ontology; step B, reasoning with SWRL; and step C, showing results

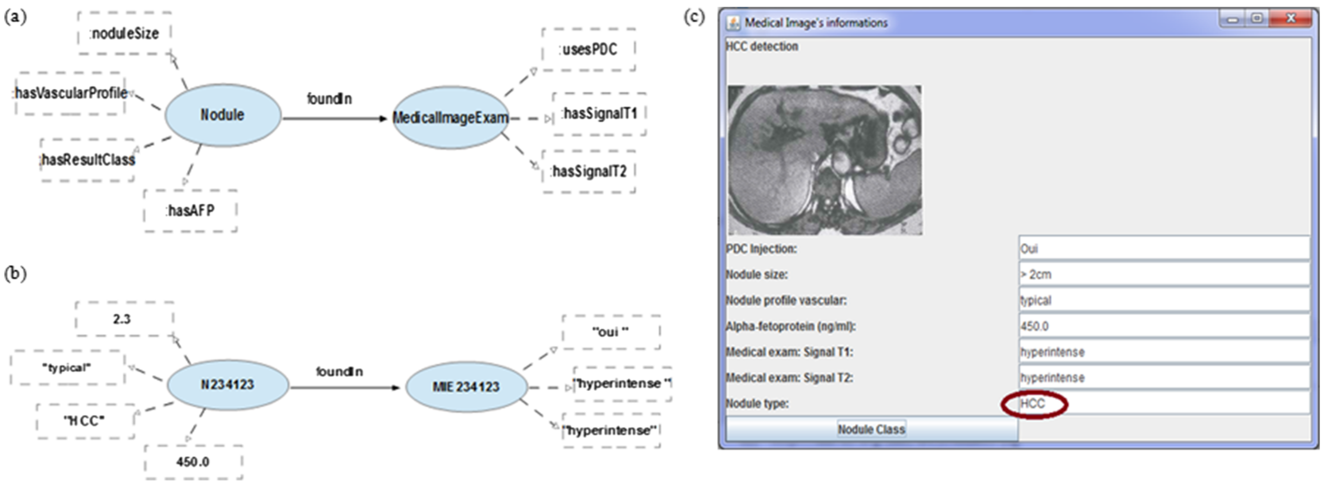

Fig. 7 SWRL rule execution for HCC detection. The applied SWRL rule provides HCC detection via medical imaging. **a** Semantic representation concepts before the execution of the rule. **b** Semantic representation concepts after the execution of the rule. **c** The result via the developed interface

ontology querying. This communication is achieved through the Jena API, which communicates with the OWL [30] file generated by Protégé.

Results and Discussion

As mentioned earlier, our proposed approach tries to exceed some previous research drawbacks. This section aims to give an interpretation of our approach by concentrating on two major parts. The first part shows our ontology metrics and some results of the proposed system with some case studies. And the second part exposes its expressivity compared to other works using a case study.

OntHCC prototype is composed of 49 classes, 166 instances, 1390 axioms, 70 rules, 53 data-type properties, and 25 object properties. In order to give more functionality to our work, we developed some graphical demonstrators to deal with different tests. Mostly, the system deals directly with the user and shows important results. Figures 7, 8, and 9 show the results of applying our proposed system with some cases studies.

To communicate with these demonstrators, we created several SPARQL rules. Figure 10 shows some examples of the used SPARQL rules. They are associated respectively to HCC nodule detection, TNM staging for HCC, and HCC treatment. The last rule gives the adequate treatment based on BCLC staging.

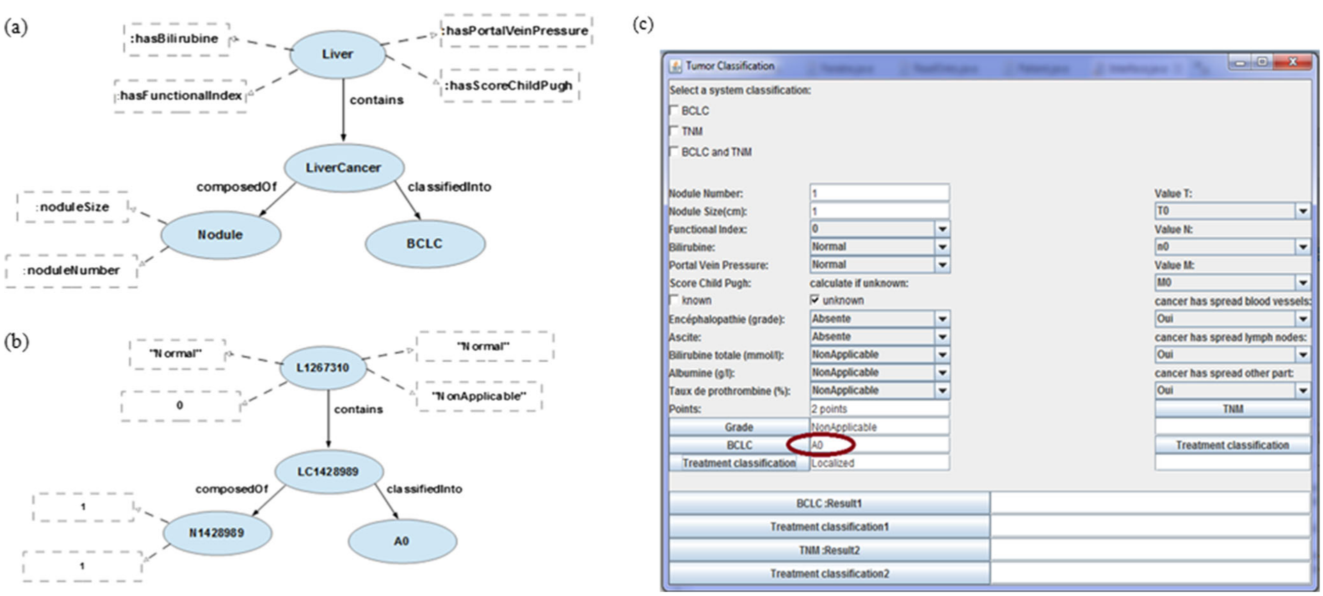

Fig. 8 SWRL rule execution for HCC staging. The applied SWRL rule provides the generation of the stage A0 according to BCLC system. **a** Semantic representation concepts before the execution of the rule. **b** Semantic representation concepts after the execution the rule. **c** The result via the developed interface

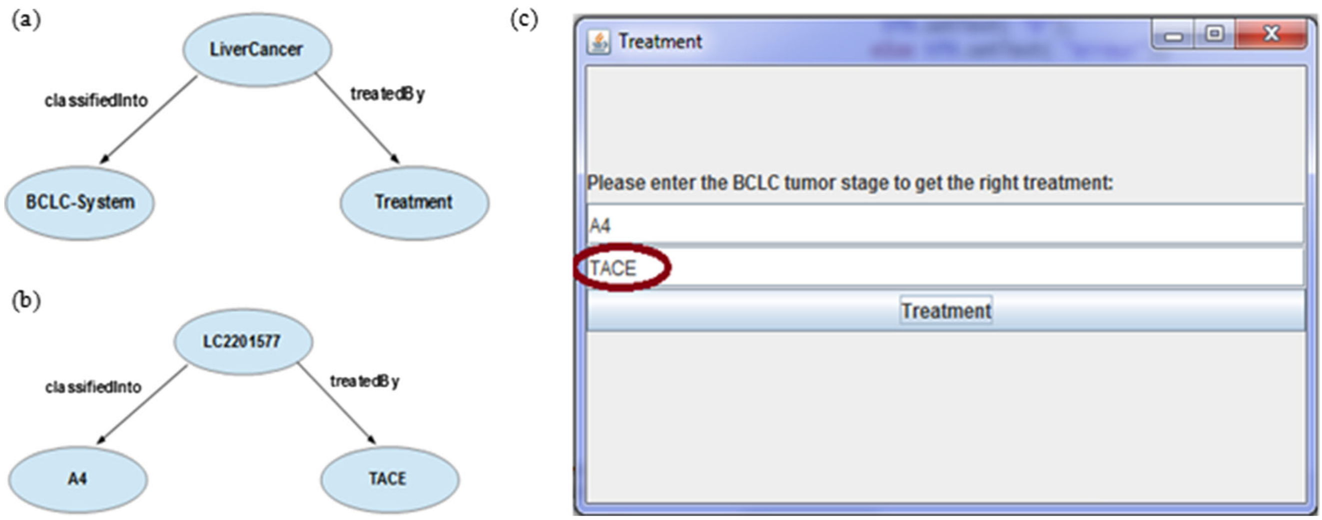

Fig. 9 SWRL rule execution for HCC treatment. The applied SWRL rule provides the treatment that can be applied to treat the lesion. **a** Semantic representation concepts before the execution of the rule. **b** Semantic representation concepts after the execution the rule. **c** The result via the developed interface

OntHCC Evaluation: Case Study

This section is intended to test OntHCC model with real medical datasets, to demonstrate the efficiency of our prototype. The first set of analyses, investigated in our work, is composed of 28 medical reports for patients who were diagnosed with liver cancer especially HCC disease. These reports characterize various patients' disease states. They describe the whole medical exam steps via clinical interpretations noted by radiologists.

To evaluate the OntHCC usefulness, we conducted a case study with a group of academics and students from our laboratory who work actually on liver tumors, imaging, and classification domain. Through this case study, we aim to assess the usefulness of our model compared to other existing models. It consists on giving the group of users a set of medical reports and four prototypes of liver ontologies. The goal is instantiating these models by different patient cases. After that, we take the generated instances to make our comparison study. Thus, to assess our approach, we follow one of the most common

(a) SPARQL query:

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX ex:<http://www.semanticweb.org/stagiaire1/ontologies/2016/5/untitled-ontology-49#>
SELECT  ?irm ?medicalimage ?medicalimageexam ?nodulesize  ?VascularProfile ?PDC ?Class ?AFP ?SignalT1 ?SignalT2
WHERE {   ?medicalimage ex:isSequenceOf ?z.
          ?irm ex:foundIn ?medicalimageexam.
          ?irm ex:noduleSize ?nodulesize.
          ?irm ex:hasVascularProfile ?VascularProfile.
          ?z ex:usesPDC ?PDC.
          ?irm ex:hasResultClass ?Class.
          ?irm ex:hasAFP ?AFP.
          ?medicalimageexam ex:hasSignalT1 ?SignalT1.
          ?medicalimageexam ex:hasSignalT2 ?SignalT2}
```

(b) SPARQL query:

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX ex:<http://www.semanticweb.org/stagiaire1/ontologies/2016/5/untitled-ontology-49#>
SELECT   ?stage
WHERE {?liver ex:contains ?cancer
          ?liver ex:hasScoreChildPugh ?score.
          ?liver ex:hasFunctionalIndex ?index.
          ?liver ex:hasBiluribine ?bilirubin.
          ?liver ex:hasPortalVeinPressure ?pressure
          ?cancer ex:composedOf ?nodule.
          ?nodule ex:noduleNumber ?number.
          ?n ex:noduleSize ?size.
          ?cancer ex:classifiedInto ?stage}
```

(d) SPARQL query:

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX ex:<http://www.semanticweb.org/stagiaire1/ontologies/2016/5/untitled-ontology-49#>
SELECT ?treatment ?cancer
WHERE {?cancer ex:classifiedInto?stage.
          ?cancer ex:treatedBy ?treatment}
```

(c) SPARQL query:

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX ex:<http://www.semanticweb.org/stagiaire1/ontologies/2016/5/untitled-ontology-49#>
SELECT   ?cancer ?stage
WHERE {?cancer ex:has-T ?t.
          ?cancer ex:has-N ?n.
          ?cancer ex:has-M ?m.
          ?cancer ex:hasSpreadBloodVessels ?x.
          ?cancer ex:hasSpreadLymphNodes ?y.
          ?cancer ex:hasSpreadOtherPart ?z.
          ?cancer ex:classifiedInto ?stage}
```

Fig. 10 SPARQL rules for OntHCC This figure exposes SPARQL rules that can be applied to interrogate the ontology. **a** Used to get information about the nodule state. **b** The stage according to BCLC stage. **c** The stage according to TNM system. **d** The type of treatment that can be applied

Table 5 Qualitative evaluation

Ontology-based approach	Concepts	Covered	Ratio
ONLIRA	11	8	72%
[28]	23	23	100%
LiCO	20	15	75%

strategies used by [48]. It is based on comparing concepts of various ontologies. We apply this technique to indicate the overall coverage of the proposed model to other models. We compare our ontology with three relevant ontologies that deal with liver cancer diseases: ONLIRA [32], ontology for liver cancer provided by [28], and LiCO [38]. From each of these ontologies, we chose the most suitable concepts with HCC detection and treatment modules. We eliminated the staging part because the majority of medical reports that we have do not provide information about tumors classification. Therefore, we did not consider staging concepts of our model in the comparison study. We choose respectively 23 concepts from [28], 20 from LiCO, and 11 from ONLIRA. Our case study consists on populating the four ontologies with instances from the medical reports. The obtained instances were collected for evaluation and comparison. For the qualitative evaluation, as mentioned in Table 5, we find that OntHCC covers 100% of the model proposed by [28]. Regarding other ontologies, we find that ONLIRA and LiCO cover respectively 72 and 75% of our model concepts. To evaluate quantitatively our model, we used only models that contain concepts not covered by our ontology. We considered instances from medical reports to realize this quantitative evaluation. Table 6 highlights ratios of this assessment. The obtained results show that quantitative ratios are greater than the qualitative ones. We can deduce that the majority of instances are related to the covered concepts. Subsequently, OntHCC is more efficient quantitatively because it contains the most number of concepts in the field of HCC detection and treatment.

For the second part of this evaluation, we used recall and precision values in order to show our model effectiveness. These values were applied to identify the relevant average of instances. We involved the generated instances to evaluate OntHCC compared to other models. The aim of these tests is to find the true and the false of the instantiated concepts. The obtained results show that our model contains the highest

Table 6 Quantitative evaluation

Ontology-based approach	Instances from covered concepts	Instances from not covered concepts	Ratio
ONLIRA	311	59	84%
LiCO	246	65	80%

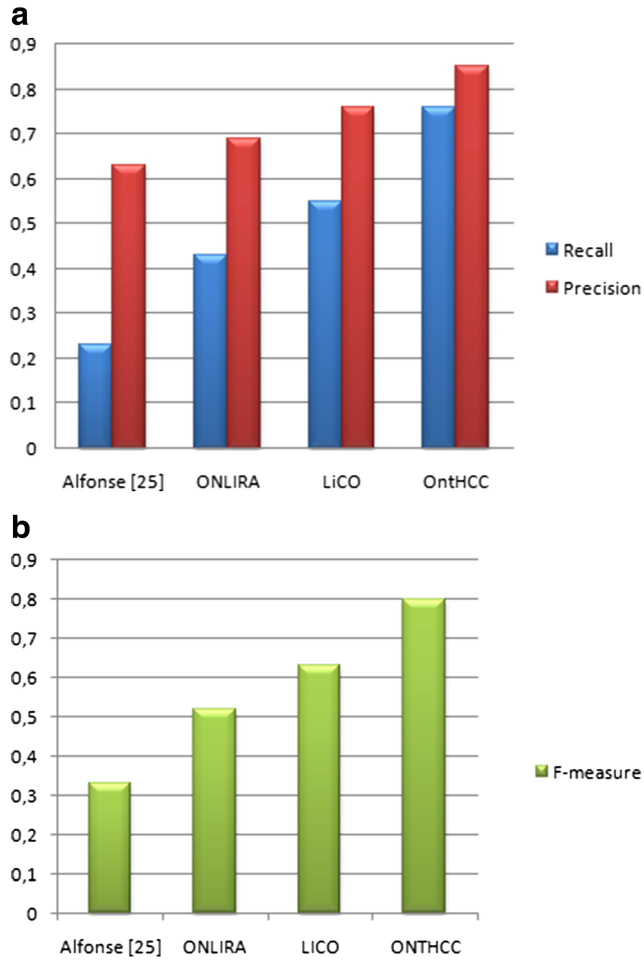

Fig. 11 **a** Recall and precision values. **b** F-measure values. Recall, precision, and F-measure are applied in this work to test our approach efficiency and the relevance percentage of the obtained results

values of recall 76%, precision 85%, and F-measure 80%. Figure 11 exposes all of these values.

To expand our evaluation, we try to compare our approach with other studies. To our knowledge, all the proposed works discuss the topic of applying knowledge representation for medical issues especially for liver disease representation. The majority of the proposed works deals with the diagnosis process of liver cancers through medical exams or imaging. They provide an ontological representation using OWL language. They aim to improve knowledge engineering achievements in medical purposes. They include ontologies for medical image interpretation such as [24, 26, 35, 39, 40]. These works focus basically on medical image features and finding. Some of these works have proposed prototypes such as OntoVIP [39], Reportviewer [26], and VHOSWS [40]. On the other hand, other works focus on the stadification process via staging systems such as BCLC [25] and TNM [28, 31, 36]. The treatment process is treated in [28, 31, 36]. Furthermore, to validate and improve the efficiency of these works, several techniques were applied such as testing with real datasets tacked mainly from clinical sources, querying and manipulating the ontology through semantic search queries (e.g., SPARQL rules, SWRL rules) [26, 31, 39] while other works try to apply standard measurements in the validation step such as recall and precision accuracies [25]. To recapitulate, despite the effectiveness of these works, few works have integrated a full semantic model. This could eventually validate the originality of our approach. In fact, it realizes three main missions: HCC detection via the medical image, HCC classification using different classification systems frequently used by radiologists such as BCLC and TNM, and HCC treatment. Moreover, our approach has the potential of integrating LI-RADS system especially in the detection phase. It could eliminate detection errors by offering additional information about the hepatic lesion. In addition, OntHCC takes the advantage of offering graphical interfaces which can be used easily by radiologists.

Conclusions

In this article, we present an ontological approach for liver cancer diagnosis. The proposed method is based on medical image description, and it can be readily used in practice. The main goal is to show an ontological model elaborated to detect liver cancer disease and especially the case of HCC. The essential features of our approach are HCC diagnosis via liver imaging. In this step, we have introduced LI-RADS system to assist on the detection process, HCC staging based on the most used classification systems in actual clinical practice, and HCC treatment. The major asset of this work is integrating essentially both modules: liver imaging and tumor staging. Also, the obtained results 76%, 85%, and 80%, respectively, for recall, precision, and F-measure suggest that the proposed approach could be useful for staging and for treatment by means of classification systems. In addition, we developed a system prototype OntHCC which demonstrates the effectiveness of our proposed approach.

Several other questions remain to be resolved in our future works. We aim to treat other medical image modalities like CT scans and creating an expanded knowledge base with a dynamic ontology. Furthermore, we should include other staging systems and the vascular profile of the MRI sequence which should be automatically calculated.

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