



18-20 APRIL 2012
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LUXEMBOURG
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Ain Shams University
Faculty Of Computer & Information Sciences

Ontology-Based Knowledge Representation for Liver Cancer

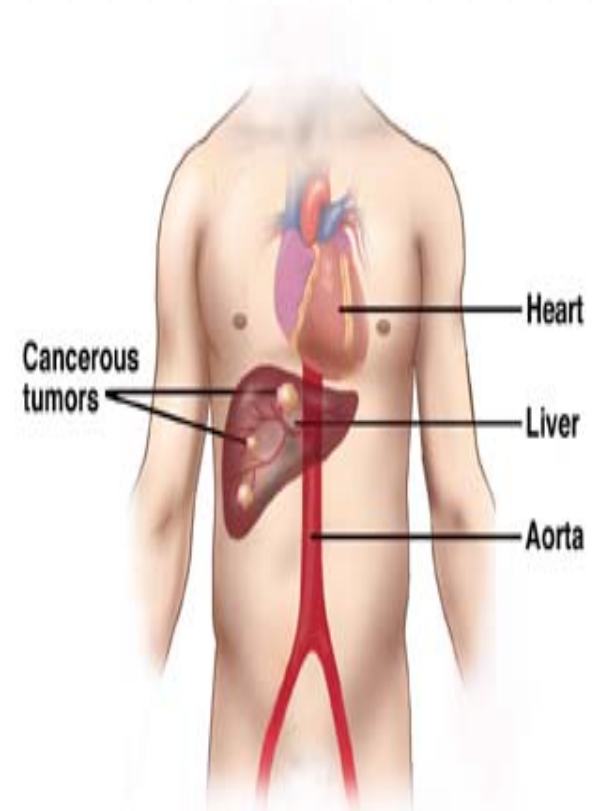
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Agenda

- Goal
- Ontology Approach.
- Medical Ontologies.
- The Liver Cancer.
- Developing Web-Based Liver Cancer Ontology.
- Conclusions.



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Goal

- o This paper presents the process of **developing a web-based liver cancer ontology**.
- o The importance of this ontology is:
 - o To **find and locate information about liver cancer** needed for interested users and domain experts.
 - o To provide a **semantic representation** of liver cancer information over the web.

Ontology Approach

- Ontology, from **philospical** point of view, deals with the nature and the organisation of reality.
- It is science of Being and tries to answer the questions:
 - *What is Being?*
 - *What does characterize Being?*
- From **AI** point of view ontology is a **shared and common understanding of some domain** that can be communicated between people and application systems.

- An Ontology is a representation vocabulary, often specialized to some domain or subject matter.
- It is a representation of a set of **concepts** within a domain and the **relationships** between those concepts.
- Its main components are:
 - **Classes** represent concepts, which are taken in a broad sense
 - **Attributes** represent properties of each concept.
 - **Relations** represent a type of association between concepts of the domain.
- An ontology together with a set of individual instances of classes constitutes a **knowledge base of any knowledge base system.**

◦ **Ontologies are now:**

- ubiquitous in many **information-systems** enterprises;
- constitute the backbone for the **Semantic Web**;
- used in **e-health**
- used in various application of **bioinformatics** and **medicine**.

◦ **Ontologies are built to:**

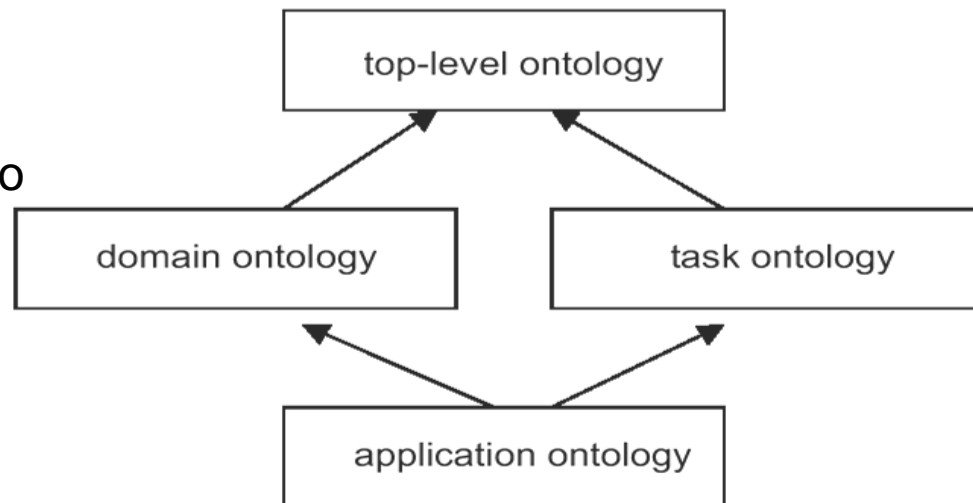
- **Share** common understanding of the structure of information among people or software agents,
- Enable **reuse** of domain knowledge,
- Make domain assumptions **explicit**,
- **Separate** domain knowledge from the operational knowledge
- **Analyze** domain knowledge.

Types of Ontologies

Describe **very general concepts**

e.g. space, time, event, which are independent of a particular problem or domain.

Describe the vocabulary related to a **generic domain**
e.g. Biology, medicine,....



Describe the vocabulary related to a **generic task or activity** e.g. Diagnosing, selling,....

Describe concepts depending both on a particular **domain and task**.

Medical Ontologies

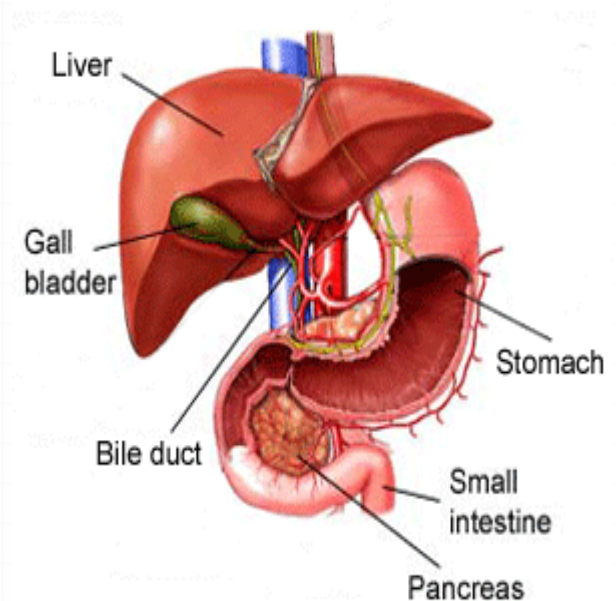
Ontology Name	Site	Purpose	Implementation Language
(1) GALEN	OpenGALEN Foundation	To allow clinical information to be captured, represented, manipulated, and displayed in a radically more powerful way . Support re-use of information to integrate medical records, decision support and other clinical systems.	GRAIL
(2) UMLS	U.S. National Library of Medicine, 22 March 2004	To link biomedical vocabularies together from disparate sources such as clinical terminologies, drug sources, vocabularies in different languages. To provide a unified terminology that can be used across multiple medical information sources.	Unknown
(3) MeSH	U.S. National Library of Medicine, 01 September 1999	Designed to show the relationship between related terms	Unknown
(4) ON9		ON9 define the ontologies: "etaontology", "semantic-fieldontology" and "structuring-concepts" in order to link the representation ontologies with the generic ontology library.	GRAIL, Ontolingua, Loom, OCML Using ONIONS methodology

(5) Tambis	Tambis (Transparent Access to Bioinformatics Information Sources) Project	Designed to provide an infrastructure that allows researchers in Bioinformatics to access multiple sources of biomedical resources in a single interface	DAML+OIL
(6) The Systematized Nomenclature of Medicine	the College of American Pathologists (CAP)	Designed to advance excellence in patient care by making health care knowledge usable and accessible wherever and whenever it is needed.	XML
(7) Foundational Model of Anatomy	Structural Informatics Group at the University of Washington, Dept. of Biological Structure & Biomedical and Health Informatics, Dept. of Medical Education and Biomedical Informatics.	Makes available anatomical information in symbolic form to knowledge modelers and other developers of applications for education, clinical medicine, electronic health record, biomedical research and all areas of health care delivery and management.	Developed using Protege-3.0 (which allows the user to develop ontologies without knowing any ontology language and export it to any language)
(8) MENELAS	European Union project, 1992-1994	Designed to allow accessing medical records in several European languages.	Unknown
(9) Gene Ontology	Gene Ontology (GO) Consortium, 2004	Designed to provide a common terminology for functional annotation of genes and gene products in biological databases	RDF(S), XML.
(10) LinkBase	Language & Computing	Designed to provide conceptual computer- understandable representation of medicine in general	Unknown

- (1) <http://www.opengalen.org/> (2) <http://www.nlm.nih.gov/research/umls/> (3) <http://www.nlm.nih.gov/mesh/meshhome.html>
(4) <http://www.ontologos.org/OML/..%5Contology%5CTAMBIS.htm> (5) <http://www.snomed.org/> (6)
<http://sig.biostr.washington.edu/projects/fm/> (7) <http://www.med.univ-rennes1.fr/menelas.html> (9) <http://www.geneontology.org/>
(9) <http://www.landcglobal.com/pages/linkbase.php0>

The Liver Cancer (hepatoma)

- Liver cancer is the **third most common cancer** in the world.
- Liver cancer is **much more common** in **developing countries within Africa and East Asia**.

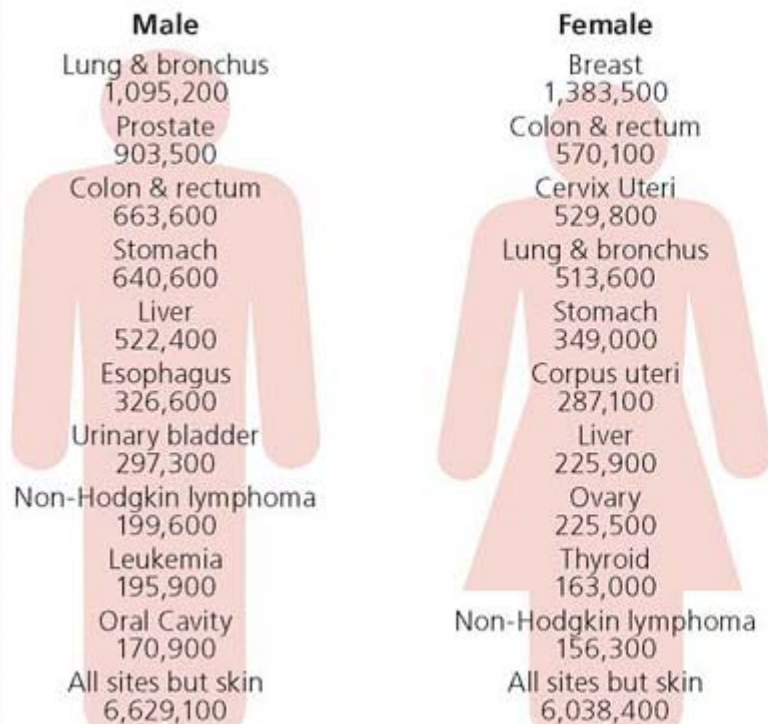


Estimated New Cancer Cases and Deaths Worldwide for Leading Cancer Sites by Level of Economic Development, 2008.

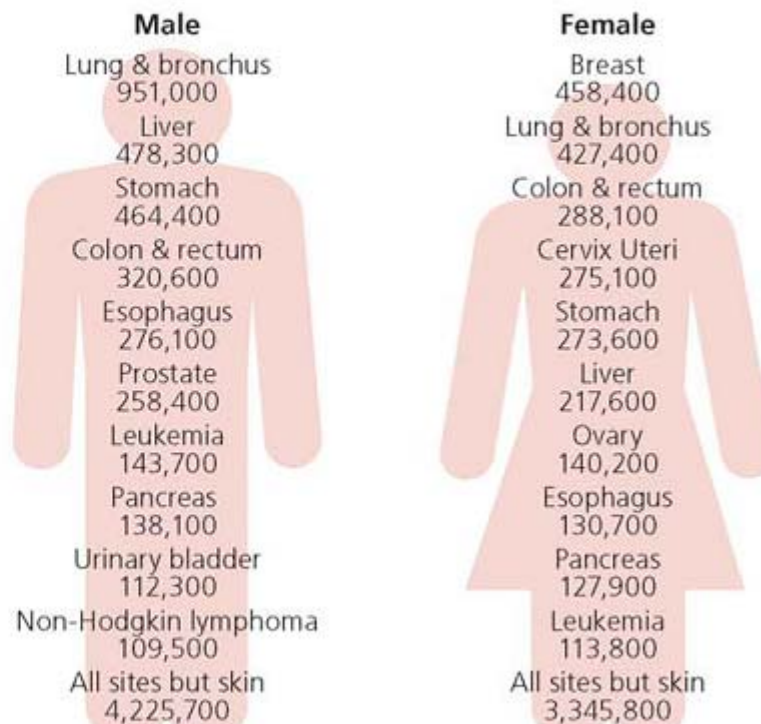
Source: GLOBOCAN 2008.

Worldwide

Estimated New Cases



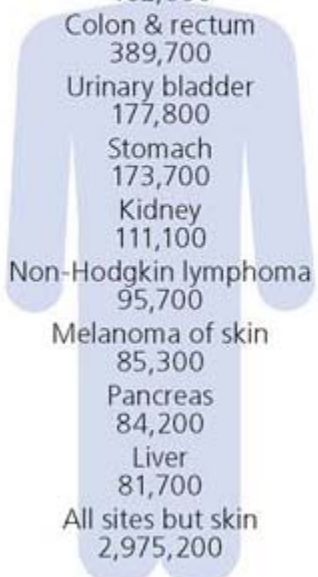
Estimated Deaths



Developed Countries

Estimated New Cases

Male



Prostate
648,400
Lung & bronchus
482,600
Colon & rectum
389,700
Urinary bladder
177,800
Stomach
173,700
Kidney
111,100
Non-Hodgkin lymphoma
95,700
Melanoma of skin
85,300
Pancreas
84,200
Liver
81,700
All sites but skin
2,975,200

Female



Breast
692,200
Colon & rectum
337,700
Lung & bronchus
241,700
Corpus uteri
142,200
Stomach
102,000
Ovary
100,300
Non-Hodgkin lymphoma
84,800
Melanoma of the skin
81,600
Pancreas
80,900
Cervix Uteri
76,500
All sites but skin
2,584,800

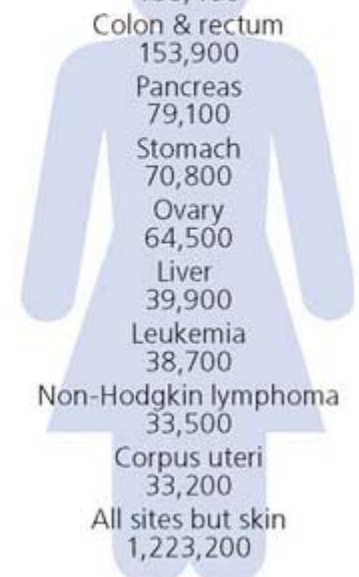
Estimated Deaths

Male



Lung & bronchus
412,000
Colon & rectum
166,200
Prostate
136,500
Stomach
110,900
Pancreas
82,700
Liver
75,400
Urinary bladder
55,000
Esophagus
53,100
Leukemia
48,600
Kidney
43,000
All sites but skin
1,528,200

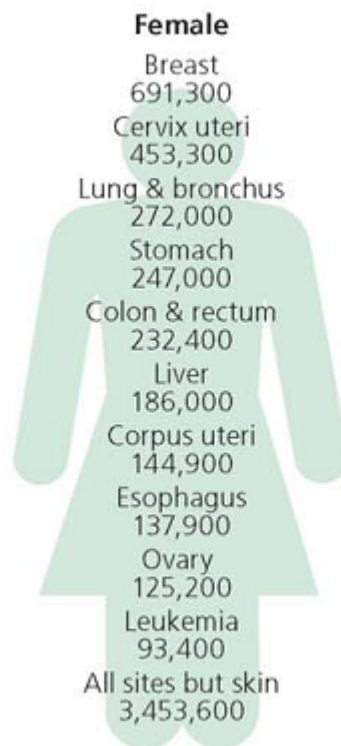
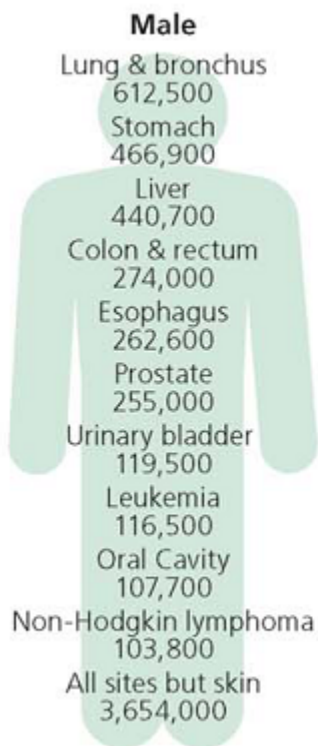
Female



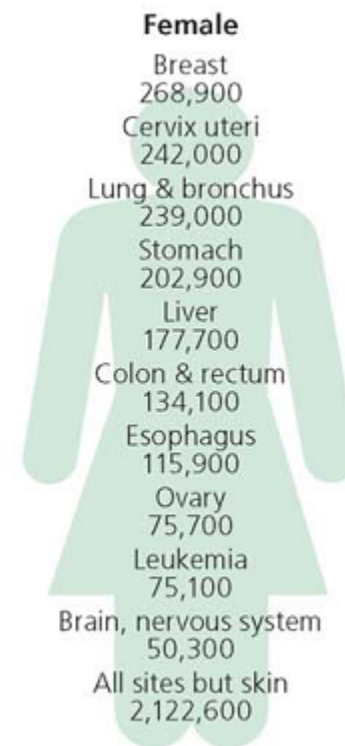
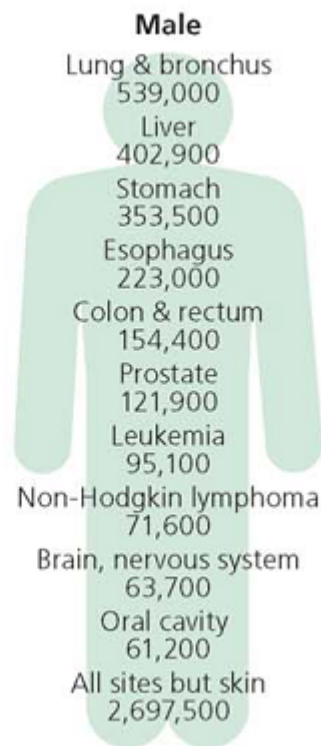
Breast
189,500
Lung & bronchus
188,400
Colon & rectum
153,900
Pancreas
79,100
Stomach
70,800
Ovary
64,500
Liver
39,900
Leukemia
38,700
Non-Hodgkin lymphoma
33,500
Corpus uteri
33,200
All sites but skin
1,223,200

Developing Countries

Estimated New Cases

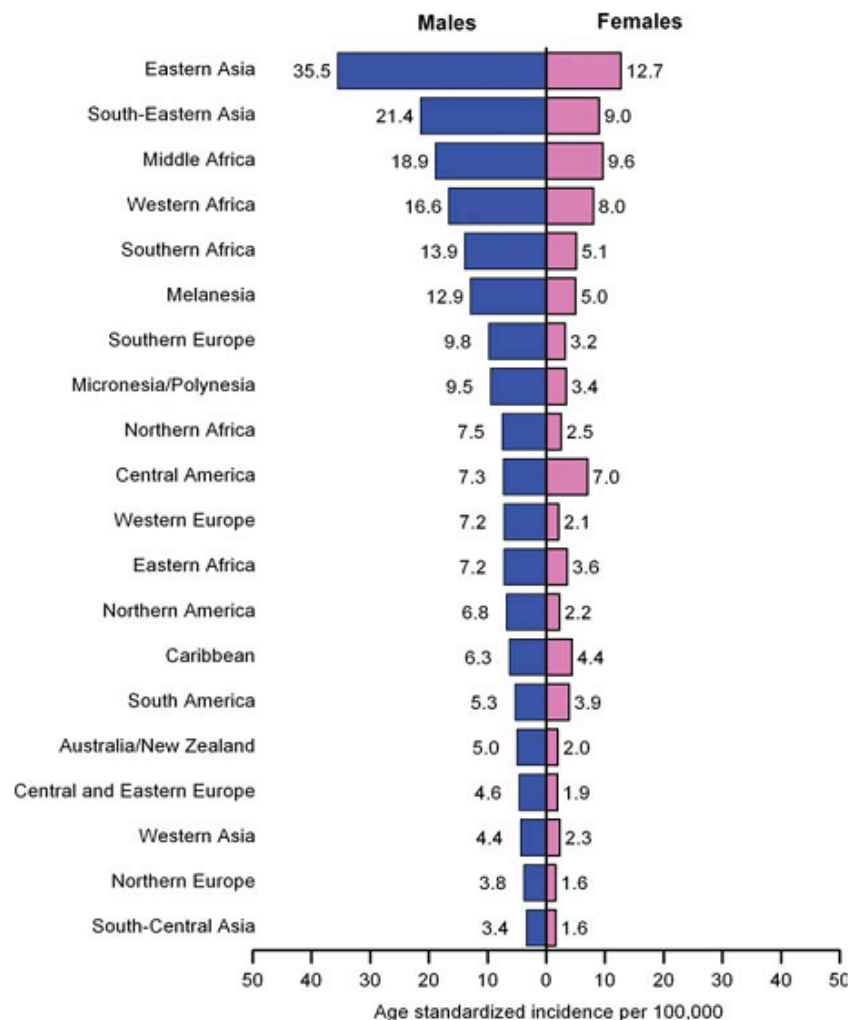


Estimated Deaths



Age-Standardized Liver Cancer Incidence Rates by Sex and World Area.

Source: GLOBOCAN2008



Deaths Associated With Liver Cancer On Rise In Egypt

THURSDAY, 14 JANUARY 2010

- President of Egypt's Liver Cancer Association Ashraf Omar reported that the number of deaths resultant from liver cancer in Egypt had risen from 4 percent in 1993 to 11 percent last year
- Omar said that "Liver cancer now has one of the highest death rates in the world"
- At a press conference following the launch of a national campaign aimed at combating liver cancer, Omar partially attributed the rise in liver cancer-associated fatalities to the lack of early detection.
- For his part, Egypt's Health Minister Assistant Abdel Hamid Abaza said the ministry was currently building a new facility for the treatment of tumors, to be equipped with the latest technology.
- Abaza said "The ministry has allocated LE400 million for tumor treatment, whether by surgery or by chemotherapy," adding that "And in the public medical insurance system, liver cancer is covered by a further LE100 million."
- Dr. Hussein Khaled, professor of tumor medicine, called for the formation of a national council mandated with fighting the scourge of cancer.
- "Smoking, drinking, pollution and fast food are among the many causes of liver cancer in Egypt," Khaled explained. "Vegetables and green tea, meanwhile, can reduce the probability of getting the disease."

- o The **subtypes** of primary liver cancer are named for the type of cell from which they develop.

Type of Liver Cancer	Description	How Common
Hepatocellular carcinoma	Hepatocellular carcinoma can have different growth patterns. Some spread tentacle-like growths through the liver. Some start as a single tumor that spreads to other parts of the liver later, as the disease develops. Others develop as nodules at several different places in the liver. Occasionally, a pattern isn't clear.	Most (about 90%) primary liver cancers are hepatocellular carcinomas.
Cholangiocarcinoma	Cholangiocarcinomas grow from cells in the bile duct of the liver. The bile duct is a thin tube that extends from the liver to the small intestine. The bile duct starts inside the liver as several smaller tubes that join together.	About 9% of primary liver cancers are cholangiocarcinomas.
Angiosarcoma	Angiosarcoma starts in the blood vessels of the liver and grows very quickly.	About 1% of primary liver cancers are angiosarcomas.

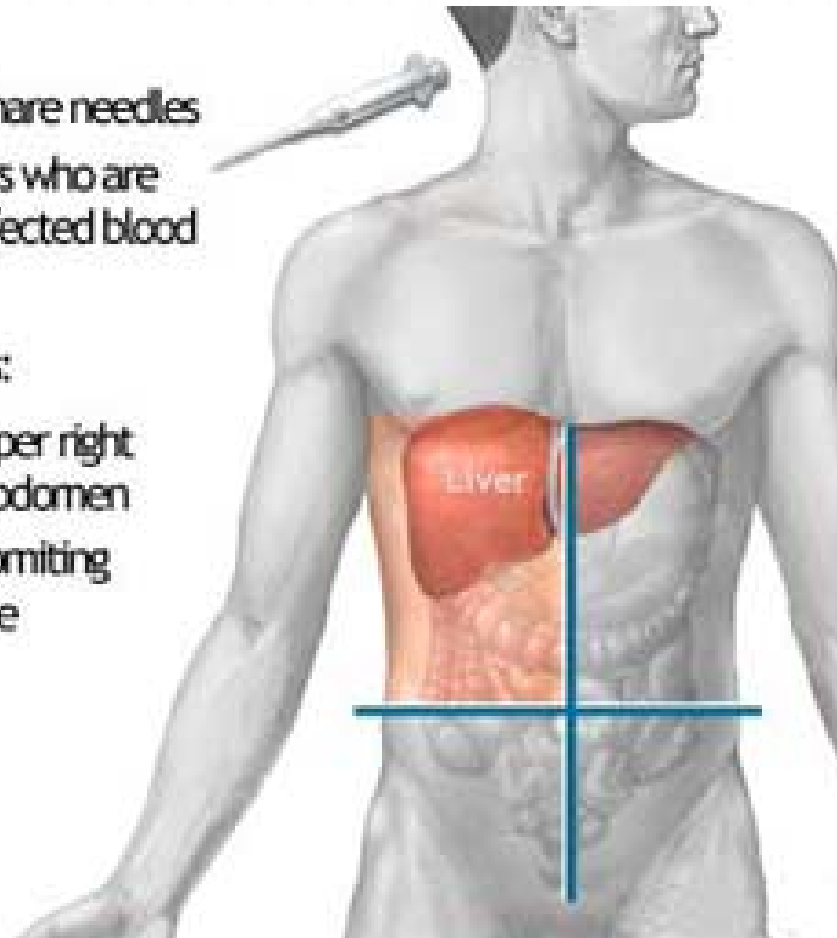
The liver cancer is described in terms of its **risk factors**, **symptoms**, **diagnosis**, **staging** and **treatment**.

Risk factors:

- people who share needles
- health workers who are exposed to infected blood

Possible symptoms:

- pain in the upper right quadrant of abdomen
- nausea and vomiting
- loss of appetite
- jaundice
- fatigue
- itching



○ Staging

- Staging is a way of **describing a cancer**, such as where it is located, if or where it has spread, and whether it is affecting the functions of other organs in the body.
- One tool that doctors use to describe the stage is the **TNM system**. **TNM** is an abbreviation for tumor (T), node (N), and metastasis (M).
- Doctors look at these three factors to determine the stage of cancer:
 - How **large** is the primary tumor and where is it located? (Tumor, T)
 - Has the tumor **spread** to the lymph nodes? (Node, N)
 - Has the cancer **metastasized** to other parts of the body? (Metastasis, M)

TNM classification of Liver Cancer

Tumor (T)

TX	The primary tumor cannot be evaluated.
T0	There is no evidence of a primary tumor.
T1	The tumor is 2 centimeters (cm) or smaller. It does not involve nearby blood vessels.
T2	Either of these: Any tumor that involves nearby blood vessels. More than one tumor, but none larger than 5 cm.
T3a	There is more than one tumor, and at least one is larger than 5 cm.
T3b	The tumor (of any size) involves the major veins around the liver.
T4	Either of these: The tumor has spread to the organs near the liver (except the gallbladder). The tumor has broken through the visceral peritoneum (layer of tissue that lines the abdomen).

Node (N)

NX	The regional lymph nodes cannot be evaluated.
N0	Cancer has not spread to the regional lymph nodes.
N1	The cancer has spread to the regional lymph nodes.

Distant Metastasis (M)

MX	The tumor cannot be evaluated.
M0	The cancer has not spread to other parts of the body.
M1	The tumor has spread to another part of the body.

- Doctors assign the stage of the hepatocellular carcinoma by combining the **T**, **N**, and **M** classifications as follows:
 - **Stage I**: The tumor has not spread to the blood vessels, lymph nodes, or other parts of the body (**T1**, **N0**, **M0**).
 - **Stage II**: The tumor involves nearby blood vessels, but it has not spread to the regional lymph nodes or other parts of the body (**T2**, **N0**, **M0**).
 - **Stage IIIA**: The cancer has not spread beyond the liver, but the area of the cancer is larger than stage I or II (**T3a**, **N0**, **M0**).
 - **Stage IIIB**: The cancer involves a major vein around the liver, but it has not spread to nearby lymph nodes or other parts of the body (**T3b**, **N0**, **M0**).
 - **Stage IIIC**: Any tumor that has spread to the organs near the liver (except the gallbladder), or if the tumor has broken through the visceral peritoneum. There is no spread to nearby lymph nodes or other parts of the body (**T4**, **N0**, **M0**).
 - **Stage IVA**: Any tumor that has spread to the regional lymph nodes but not to other parts of the body (**any T**, **N1**, **M0**).
 - **Stage IVB**: Any tumor that has spread to other parts of the body (**any T**, **any N**, **M1**).

Developing Web-Based Liver Cancer Ontology

1. Organizing and Scoping

- Determining the objectives.
- Defining the boundaries of the ontology.

2. Data Collection

The raw data needed for ontology development is acquired.

- MedicineNet
- Cancer.Net
- The National Cancer Institute (NCI)

3. Data Analysis

- Define the **classes** and class hierarchy.
- Define the **properties** of classes (slots)
- Define the facets of the slots
(e.g. domain and range of a slot, cardinality, slot-value type)
- Create individual **instances** of classes.

With the help of expert physician in that domain

4. Initial Ontology Development

A preliminary ontology is developed (initial implementation)

- Language: OWL-DL
<http://www.w3.org/TR/OWL-ref/>
- Tool: Protégé-OWL
- Approach: Top-Down

5. Ontology Refinement

The initial development is iteratively refined.

Results: The Liver Cancer Ontology Classes



- The liver cancer ontology has three main classes;
- **Disease**: contains the *LiverCancer* class with its types.
- **Medical_Intervention**: contains the *Staging*, *Diagnosis* and *Treatment* classes.
- **References**: contains the *Symptoms*, *Stage*, *Risk_Factors* and *TNM_System* classes
- Each one of these classes may have its own subclasses according to the structure of the liver cancer.

The Object Properties of Liver Cancer Ontology

Property	Domain	Range	Type
hasCauses	Hepatocellular Carcinoma	Risk_Factors	
hasSymptoms	Hepatocellular Carcinoma	Symptoms	
hasStage	Hepatocellular Carcinoma	Stage	Functional
diagnosedBy	Hepatocellular Carcinoma	Diagnosis	
treatedBy	Hepatocellular Carcinoma	Treatment	
stagedBy	Hepatocellular Carcinoma	Staging	
has_T	Stage	T	Functional
has_N	Stage	N	Functional
has_M	Stage	M	Functional

The Instances of the Classes of the Liver Cancer Ontology

Class	Instances
Diagnosis	Angiogram, Biopsy, Blood_tests, CT_scan, MRI, Physical_exam, Ultrasound_test
Staging	Bone_scan, CT_scan_of_the_chest, PET_scan
Treatment	Ablation, Chemoembolization, Chemotherapy, Cryoablation, Hepatectomy, Hepatic_arterial_infusion, Targeted_Therapy, Immunotherapy_therapy, Liver_transplant, Proton_beam_therapy, Radiation_Therapy, Radioembolization, Stereotactic_radiosurgery, Surgery
Risk_Factors	Aflatoxin, Alcohol, Cirrhosis, Hemochromatosis, Hepatitis_B, Hepatitis_C, Iron_storage_disease, Obesity_and_diabetes
Symptoms	A_lump_or_a_feeling_of_heaviness_in_the_upper_abdomen, Fever, Loss_of_appetite_and_feelings_of_fullness, Nausea_and_vomiting, Weight_loss, Pain_in_the_upper_abdomen_on_the_right_side, Swollen_abdomen, Weakness_or_feeling_very_tired,
T	TX, T0, T1, T2, T3a, T3b, T4
N	NX, N0, N1
M	MX, M0, M1

Conclusions

- This paper presents the process of developing a **liver cancer ontology**.
- This ontology was built using the **Protégé-OWL** editing environment and encoded in **OWL-DL** format.
- This ontology can be used by **experts** or **medical researchers** who want the **liver cancer knowledge** to be represented in a **semantic way** that allows **reasoning capabilities**.

Thank You