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INTERNET OF MEDICAL IMAGING THINGS AND ANALYTICS IN SUPPORT OF PRECISION MEDICINE FOR EARLY DIAGNOSTICS OF THYROID CANCER*

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Abstract. In this paper the role of advanced information technologies such as Internet of medical imaging Things and analytics in support and promotion of precision medicine is revealed considering a case study of early thyroid cancer diagnostics. The concept of precision medicine is presented and analyzed from the point of view of computational science and the new paradigm for scientific research. The focus of the paper is on the intersection of Internet of medical imaging Things and analytics ecosystem and precision medicine. The computational flow of *in silico* knowledge data discovery is presented and analyzed and the beneficial outcomes for the case study of thyroid cancer diagnostics revealed. Finally,

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Key words: Internet of medical imaging things and analytics, thyroid cancer diagnostics, ultrasound imaging.

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the architecture of experimental framework for *in silico* knowledge data discovery is proposed based on thyroid cancer imaging analytics.

1. The problem area. In the Digital Era, modern society faces the challenges of advanced knowledge that technology helps us create. Advanced information and communication technologies facilitate the efficiency of scientific research in all areas—life sciences, technology, and humanities. The computational paradigm in scientific research involves computer-based models and simulations (*in silico* experimentation) that offer greater potential and facilities for investigation than theoretical analysis does. Globally, this resulted in the accumulation of huge amounts of *in silico* experimentation data that can be subjected to analysis in order to extract value. The fourth scientific research paradigm – Data Intensive Science Discovery – revolutionized fundamental and applied scientific research [1, 2]. Innovative modern technologies, such as Big data analytics, Internet of Things, cloud computing, give researchers powerful opportunities for Knowledge Data Discovery and intelligent decision making [3, 4, 5, 6]. Personalizing patient treatment is a difficult and expensive task and instead, in the case of precision medicine, patients are grouped according to their specifics and are assigned treatment optimal for their target group. The main objective of the Precision Medicine Initiative is individualized healthcare. The deployment of precision medicine into patient care involves considering three crucial factors: genetic specifics, environmental factors and individual lifestyle.

Precision medicine [7] is one of the hottest topics nowadays and involves disease treatment that takes into account the individual genetic profile, environmental specifics, and lifestyle of the individual. In 2015, US President Barack Obama launched the Precision Medicine Initiative with the aim to improve health and disease therapy by means of tailoring the treatment and prevention strategy to fit the specifics of the individual patient in lieu of the "one-size-fits-all" approach (average patient). "Doctors have always recognized that every patient is unique, and doctors have always tried to tailor their treatments as best they can to individuals", President Obama noted in his State of the Union address [8].

Cancer is a severe disease that progresses in many forms. All of these are described in multiple subtypes. One particular type is thyroid cancer.

As with most other types, early diagnostics is a key factor in successful treatment. One of the ways for its timely detection is imaging diagnostics. Visually, changes in the thyroid gland are recorded through ultrasound examination of the patient. Due to the large amount of data accumulated in it, considering the number of patients, it is necessary to introduce automated methods for the analysis of sonographic images. Already many approaches have been tested for this purpose—Artificial Neural Networks, Bayes Networks, Decision trees, Support vectors, and so on.

The results obtained from automated analytics need to be presented in a compact form. In it, they can later be validated and presented in a handy appearance for the medical staff. They can also be distributed among different healthcare institutions (clinics, hospitals, institutes) for educational and research purposes, published in specialized online and offline editions, and archived for a long time. This provides an opportunity for future comparison with newly received data for the same patient in assessing the development of his/her health status. It is also possible to combine them with other information obtained from different types of built-in biosensors, recording many other indicators, for a more detailed picture of the patient's condition.

In this paper the IoT ecosystem and its intersection with an analytics ecosystem and healthcare is presented. The specifics and classification of imaging data with respect to thyroid cancer diagnostics are discussed. Finally, an experimental framework for medical imaging analytics and *in silico* knowledge data discovery for the purpose of early detection of thyroid cancer is proposed.

2. The Intersection of Internet of medical Things and analytics ecosystem and healthcare. In contrast with the current fragmented healthcare, the interconnection model of the IoMT ecosystem [9, 10] contributes the possibility of updating the medical crew on the most promising treatment scenario by the extensive support of Internet of Things (IoT) (Fig. 1).

The latter makes it possible to enable uninterruptable monitoring without medical personnel being present and waving proper alarms when needed. Geographical position is no longer an obstacle before placing a correct diagnosis, effective superintendence and adaptive treatment. The patient is given the possibility to send data of his/her own health status. In addition to this new functionality, by the application of various connected devices, IomT is the mean for introducing personalized care over a large number of patients. This new care delivery model assures optimizing the care costs by promotion of preventive and proactive medical actions rather than taking only reactive measures.

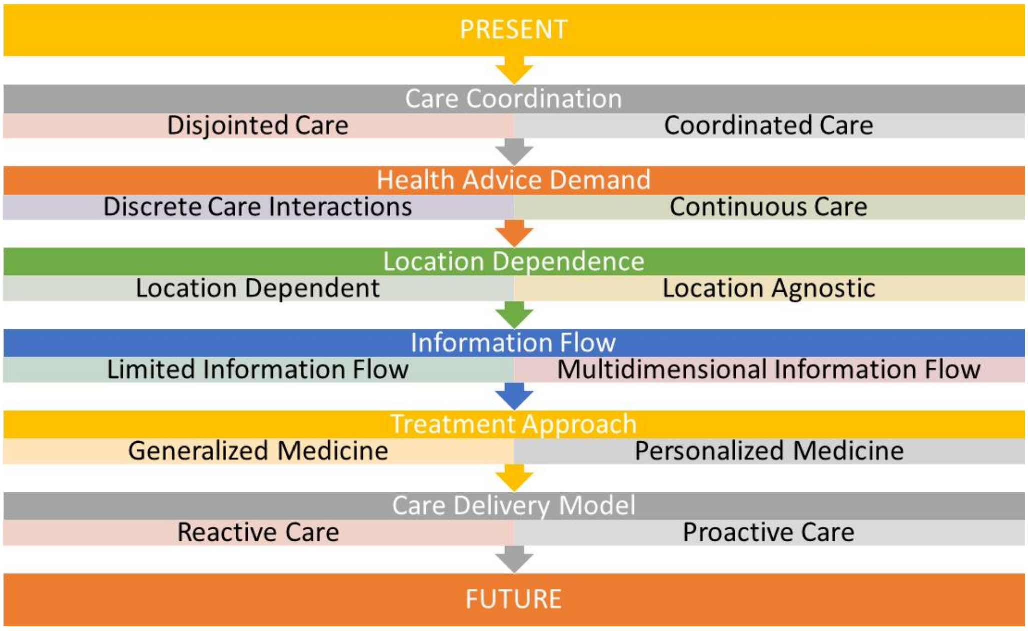


Fig. 1. The intersection of Internet of medical things ecosystem and analytics and healthcare

The space of connected devices, which lays grounds for the wide variety within the Internet of Things (IoT) with medical application, may be represented in the following groups [11]:

- invasive devices—blood analyzers, immune-assays, breast biopsy equipment, HIV detection systems;
- physiological monitors—weighing scales, pulse oximeters, BP meters, ECG, ventilators, blood glucose meters and heart rate monitors;
- mobile medical applications—medication adherence systems, dosage calculation systems;

- wearables—activity tracker, pedometer, sleep apnea detector;
- capital intensive devices—implants, prostheses, MRI/CT/Ultrasound scanners.

The Internet of Medical Imaging Things (IoMIT) is the next step towards expanding the ever-growing role of medical imaging devices by interconnecting them in a unified network environment. Apart from classical medical imaging techniques, such as Magnetic Resonance Imaging (MRI), Computer Tomography (CT) and Ultrasound Imaging (US), two new modalities emerge recently which deserve attention—Digital Breast Tomosynthesis (DBT) and 3-D Ultrasonic Holography [12, 13, 14, 15]. The first technique provides better lesion visibility leading to better performance in early cancer diagnosis.

A series of images are obtained along the breast helping for more detailed spatial reconstruction. The second approach does not employ dangerous radiating emissions, making it a preferred solution for preventive and post-operative examination. The achieved resolutions are higher than those registered by ordinary ultrasound imagers. Computer-based data interpretation is better as a consequence of this enhancement.

One of the most successful solutions for healthcare industry in the IomT-enabled infrastructure is the mobile applications for remote health monitoring system, i. e., the Digital Health Advisors that facilitate communications between patients and doctors over a secured connection.

Wireless body area network (WBAN), also called body sensor network (BSN), actually make it possible to acquire and accumulate personal medical data out of a wide spectrum of wearable devices (physiological biosensors), embedded in or on the surface of the body or suitable for wearing in clothes, bags, etc. The data acquired *in situ* about the physiological status of a person is transmitted via Internet and thus is made accessible in reasonable time and in a secure way to doctors regardless of the patient's location.

The concept of interconnecting and remote monitoring of medical imaging equipment over the Internet dates back to approximately 20 years ago. The Big Three medical imaging companies Siemens Healthcare, Philips Healthcare and GE Healthcare built up together a strategy for establishing "All-in-one Health Cloud" in 2015 [16, 17, 18]. The major aim is to move computer-intensive image processing to the Health Cloud ecosystem. According to HealthIT Analytics (Intelligent Network Media), imaging analytics is "the first step to personalized medicine" [19, 20].

Signal processing is playing an increasingly important role in modern times, mostly due to the ever-increasing popularity of IomT devices. Analysis of IomT data in medicine helps doctors to make a reliable and accurate disease diagnosis and prognosis, for predicting disease progression and the effect of treatment as well as for drug target identification.

Medical imaging refers to techniques and processes used to create images of various parts of the human body for diagnostic and treatment purposes within digital health [11]. Medical image in healthcare helps early diagnostics of diseases and prescribing more effective therapy [21, 22].

Internet of medical imaging Things is an important subarea of IomT technologies and is of crucial importance for imaging diagnostics. Euro-BioImaging European Research Infrastructure for Imaging Technologies in Biological and Biomedical Sciences (Euro-BioImaging, EuBI) will provide open access for users to a wide range of state-of-the-art Biological and Medical imaging technologies for biologists in Europe and beyond [23]. It will offer support and training of imaging data for users and infrastructure providers and will continually evaluate and incorporate new imaging technologies to provide state-of-the-art services in a sustainable way such as image data repositories and analysis tools. EuBI will consist of a set of complementary, highly interconnected and geographically distributed nodes – special image processing devices – to reach European scientists in all Member States. The infrastructure will be managed by a strong supportive and coordinating organization that is at the center of EuBI. The Hub will provide the virtual access point from which users will be targeted to their desired image technology by serving the relevant EuBI nodes. The Center will coordinate data management and training activities tailored to the needs of users of the imaging infrastructure.

Next to genomics, medical images are one of the fastest growing Big clinical data sources in the healthcare space. The amount of storage volume needed to house medical images has more than tripled since 2005, and is projected to double up as a sustainable trend in the near future. So, healthcare facilities are more often looking to the cloud to ensure high-capacity medical image storage. Medical imaging cloud technologies offer web-based imaging analytics platforms. Cloud imaging services comprise ultra-fast cloud computing (supercomputing) infrastructures, advanced visualization, deep learning and cloud medical imaging storage and sharing. The conceptual model of Internet of medical Things and analytics ecosystem is presented in Fig. 2.

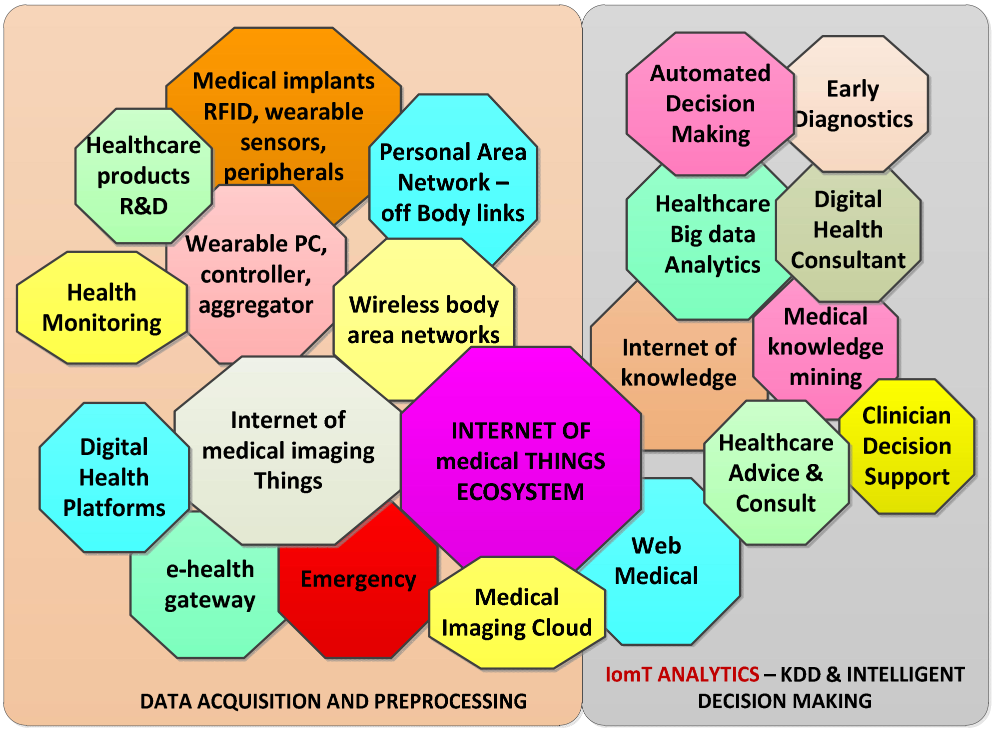


Fig. 2. The conceptual model of Internet of medical Things and analytics ecosystem

The cloud-based technology platform Medimsight [24] is a cloud marketplace offering picture archiving and communication systems (PACS) services running over the Google cloud infrastructure providing secure, unlimited, fast and affordable (*free* for research) cloud services with an open API to integrate with other vendors at all levels, including AI analysis, storage and analytics.

On the diagnostic imaging side, deep learning will facilitate selecting and extracting features from medical images as well as constructing new predictive ones [25]. IBM Watson recently boosted itself with more than $4 billion worth of new assets through the acquisition of Phytel (population health), Explorys (cloud), Merge (imaging), and Truven (analytics). Obviously, collecting and accumulating patient-generated health data from IomT devices is a key to population health management healthcare. Big data analytics becomes a key competency for society to acquire the necessary competency to ensure high quality patient care. Typical Electronic Health Records (HER), such as RxNORM, LOINC, DICOM, and SNOMED CT, are now being put to deep semantic analysis in order to extract general profile knowledge. Thus, the Internet of Knowledge (IoK) emerges as the next stage in generalizing medical data placing the accuracy of early diagnosis to higher levels.

All the data registered by various sensors within IoT, most of which employ embedded design, needs to be entered into a unified environment and further properly formatted and processed [25]. Prior to that, means for visualization and source processing in the form of client applications considering both the Quality of Service and power efficiency also should be interconnected with their related information to this framework.

3. Imaging data specifics and classification for thyroid cancer diagnostics. Thyroid cancer diagnostics is based on ultrasound image analysis using Thyroid image reporting and data system (TI-RADS) [26, 27]. Thyroid lesions are classified based on the risk stratification system TI-RADS approved by the American College of Radiology (ACR). There is also a standardized scoring system for diagnosis. Sonographic TI-RADS include the elements TI-RADS 1–6, the first of which corresponds to a normal thyroid gland, followed by benign lesions, then probable benign lesions, suspicious lesions, probably malignant lesions and finally biopsy-proven malignancy. In TI-RADS 2 echogenic specks are observed of colloid type I, typical for avascular anechoic lesions as well as non-encapsulated nodules embodied in colloid type II peripheral halo and expansile vascular nodules (colloid type III)—all of them pose no risk of malignancy. Hyperechoic, iso-echoic and hypoechoic nodules appear, sometimes with partially formed capsule or peripheral vascularity, in TI-RADS 3 category. Here the risk of malignancy is less than 5%, still the lesions are mostly benign. TI-RADS 4 is divided into three sub-categories—4a for one suspicious feature, 4b for two and 4c for three or four. TI-RADS 5 includes all five suspicious features. These features are solid component, markedly hypoechoic nodule, microlobulations or irregular margins, microcalcifications, and taller-than-wider shape. The associated risks of malignancy are 5–10%, 10–80% and more than 80% respectively by increment of the category.

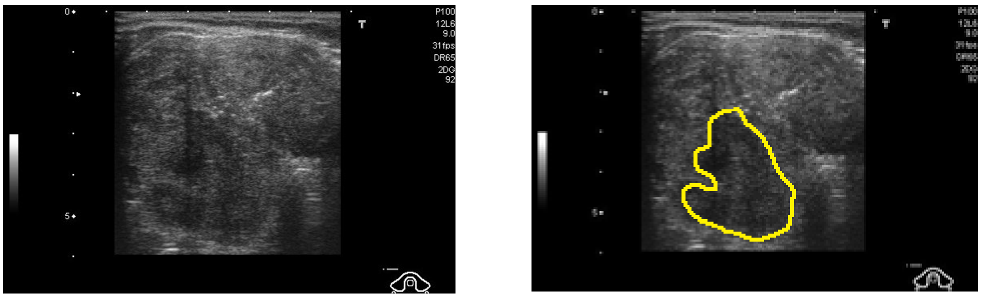
ACR proposed TI-RADS uses reporting system for the observed thyroid nodules. It is a standardized scoring system (Table 1), which helps on making recommendations for fine needle aspiration (FNA) or additional ultrasound imaging at a later stage. One score is taken from each category. When multiple nodules, typically more than four, are observed, then only four with the highest scores are reported and possibly followed up. The relation between scoring and classification is: TR1 0 points—benign, TR2 2 points—not suspicious, TR3 3 points—mildy suspicious, TR4 4–6 points—moderately suspicious, and TR5 ≥ 7 points—highly suspicious. FNA is not recommended for TR1 and TR2. Follow up is required in 1, 3 and 5 years for sizes ≥ 1.5 cm at TR3 and ≥ 1.0 cm at TR4 (in 2 years as well), also for ≥ 0.5 cm at TR5 where annual follow-up is required for up to 5 years. FNA is recommended for all these cases for sizes ≥ 2.5 cm, 1.5 cm and 1.0 cm respectively.

Table 1. Ultrasound findings scoring in five categories [26, 27]

Composition (choose 1)	**Echogenicity** (choose 1)	**Shape** (choose 1)	**Margin** (choose 1)	**Echogenic Foci** (choose all that apply)
Cystic or almost completely cystic—0 points	Anechoic—0 points	Wider than tall—0 points	Smooth—0 points	None or large comet tail artefact—0 points
Spongiform—0 points	Hyperechoic or isoechoic—1 point	Taller than wide—3 points	Ill-defined—0 points	Macro-calcifications—1 point

Mixed cystic and solid—1 point	Hypoechoic—2 points		Lobulated/irregular—2 points	Peripheral/rim calcifications—2 points
Solid or almost completely solid—2 points	Very hypoechoic—3 points		Extra-thyroidal extension (ETE)—3 points	Punctate echogenic foci—3 points

Thyroid image databases. Pedraza et al. [27, 28] presented recently an open access thyroid ultrasound-image database. It is a result of an examination of 299 patients—270 females and 29 males at average age of 57.35 years with deviation of ±16.2 years. All obtained images are in uncompressed JPEG format, annotated after diagnosis according to the TI-RADS requirements. A specially designed annotation tool was used to classify the different cases, such as thyroiditis, cystic nodules, adenomas and thyroid cancers. Accurate lesion delineation is then included in XML format. In addition to the initial diagnosis, malignant lesions are confirmed by biopsy. Finally, 347 images compound the Thyroid Digital Images Database—TDID. A sample image from the database is shown in Fig. 3.



a) original b) annotated

Fig. 3. Thyroid ultrasound image from the DDTI

One of the earliest databases of thyroid images has been collected at the Garavan Institute, Sydney, Australia [29] as a sequence of 10 sub-sets. The number of instances is 7200 with 21 attributes present. They are either

Boolean or continuously values covering 2800 training instances and 972 test ones. The researchers who gathered the data consider it suitable for training Artificial Neural Networks (ANNs).

TCIA Collections [30, 31] is extensive database of images and related clinical data of patients with various types of cancer. It is accessible for public download after de-indentification from personal details, typically in DICOM format. Thyroid cases are represented by CT and PET modalities for six patients after seven studies. There are 28 series comprising 2780 images with a total size of 1.16 GB.

4. Experimental framework for medical imaging analytics and *in silico* knowledge data discovery for the purpose of early thyroid cancer detection. The intersection of Internet of medical imaging Things and analytics and precision medicine lies in *in silico* knowledge data discovery (*in silico* KDD) that makes possible the design and deployment of smart digital consultants helpings clinicians and researchers to make accurate disease diagnostics and prescribing the optimal therapy for an individual patient, especially for the case study of cancer.

The computational workflow encompasses the stages of a standard computational pipeline for data analytics and knowledge data discovery: data acquisition and modeling, preprocessing stage (filtering, problem dimensionality reduction, multiple sequence alignment, signal processing), data analytics stage and postprocessing stage including result visualization and interpretation and experts' estimation of interest (Fig. 4). For the purpose of *in silico* knowledge data discovery, quantitative as well as qualitative types of data analytics have to be conducted.

Descriptive analysis is conducted by means of data mining tools and at this stage of the computational pipeline the training and validating data sets are being built up. Then the diagnostic analysis is performed, the outcome of which is, for example, finding out the specific genetic disorder. The predictive analysis follows, which prognosticates the progress of the disease. For the case study of early thyroid cancer diagnostics, cancer malignancy and life duration are being predicted.

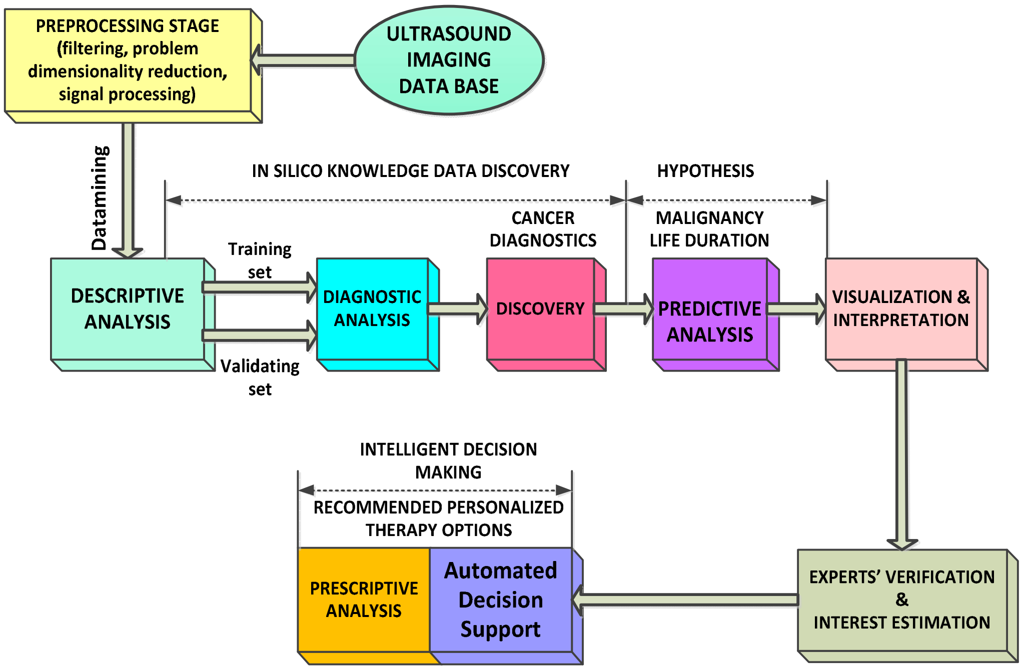


Fig. 4. *In silico* knowledge data discovery pipeline for the case study of early thyroid cancer diagnostics

Based on the current state of the Internet of Medical Imaging Things and contemporary classification techniques [32] we propose an experimental framework for *in silico* knowledge data discovery for early detection of thyroid cancer (Fig. 5).

The proposed experimental framework includes Deep learning framework Caffe and Tensor Flow used for training the Machine Learning model and mobile application that uses this trained model and the built-in camera for analysis of medical images. The framework lays the foundation for personal medical consultant apps which will enable the patient to pre-diagnose symptoms or verify the doctor's diagnosis [32].

All ultrasound images are subject to pre-processing where contrasting enhancement, intensity correction, noise filtering, and dimensions correction are implemented.

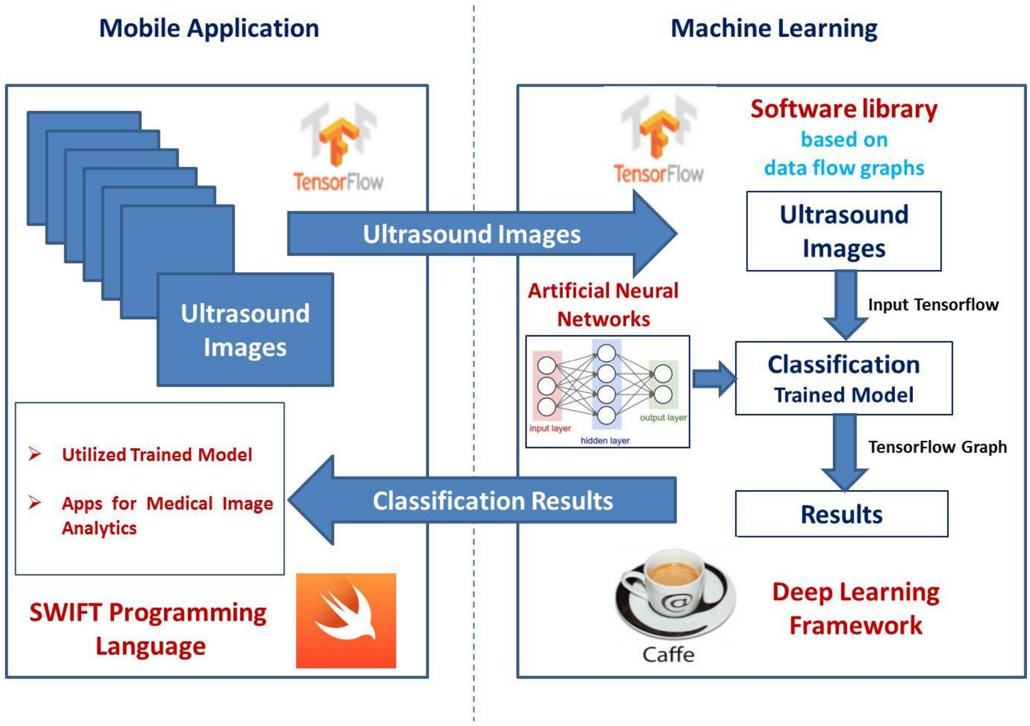


Fig. 5. Experimental framework for *in silico* knowledge data discovery for early thyroid cancer diagnostics

The software library TensorFlow and Caffe framework is the other essential part of the proposed experimental framework. The computational library TensorFlow is developed by Google Inc.; it is intended for accelerated calculations using graphs and tensors [33]. In this instance, different configurations of the ANN could be accommodated for the various types of lesions observed in the thyroid. Massive parallelization using multiple CPUs and GPUs and the support of dedicated API for data exchange are part of the qualities which characterize this library.

Caffe is a deep-learning framework made with expression, speed, and modularity in mind. It is an expressive framework which encourages application and innovation. Models and optimization are defined by configuration without hard-coding [34].

The machine-learning approach applied in the proposed experimental framework is Artificial Neural Networks (ANNs) because of the best results obtained for the case study of pattern recognition. The objective of ANNs is to make computers "think" and solve issues as human beings do, especially for making decisions in cases where a rule based approach is not applicable. ANNs offer a promising approach to analyzing big medical imaging data in an effective manner.

5. Conclusions. In this paper the role of Internet of medical imaging Things and analytics in support of precision medicine for early thyroid cancer diagnostics was presented. The Internet of medical imaging Things analytics ecosystem and its intersection with precision medicine was discussed with respect to the new paradigm for scientific research. Finally, the architecture of an experimental framework for *in silico* knowledge data discovery was proposed, based on medical imaging analytics for early thyroid cancer diagnostics.

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