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Interoperable Medical Application for CTC Counting

Victoria M. Cal-González[a], Lorena González-Castro[a b]

[a] Department of eHealth, Galician Research & Development Center in Advanced Telecommunications, Vigo, Spain
[b] University of Vigo, Spain

Abstract

In the present poster we will explain how the development of an interoperable AI-powered application for Circulating Tumor Cells (CTCs) counting is addressed. We will explain the selection of the most appropriate information for early detection of distant metastasis, local recurrence and the data structure definition to be compliant with international standards and ontologies.

Keywords:

Neoplastic Cells, Circulating; Decision Support Systems, Clinical; Health Information Interoperability

Introduction

The objective of PERSIST is the development of an open and interoperable ecosystem to improve the care of **breast and colon cancer** survivors. The ecosystem proposed consists of a **Big Data platform** to be built on top of an open infrastructure. One of the main innovations of PERSIST is the contribution to establish evidence on the **use of liquid biopsy** techniques [1], [2] to the follow-up of cancer patients. In this regard, a software for CTC counting enabled through a web application will be developed to reduce the time spent on **identifying and counting the target cells** in the images generated by a confocal microscope from patients' blood samples.

Methods

Information Selection

Liquid biopsy flourished in recent years as a powerful technology that can provide accurate prognosis, personalised treatment and earlier diagnosis of metastasis at lower costs [3],[4]. Specifically, the circulating tumour cells (CTCs) have demonstrated clinical significance [5]. The separate analysis of their different types is also a valuable source of knowledge. As general classification, the CTCs can be divided into epithelial (E-CTC), epithelial-mesenchymal (EMT-CTC) and mesenchymal (M-CTC) types. Equally, HER2-level measurement also possesses a well-known role in breast cancer. In this first phase, the web application will focus on general CTC, however it will add incrementally the rest of the information following an agile methodology.

Output structure

While other systems are being designed with a privative and commercial intention, PERSIST ensures the effectiveness of the proposed framework by providing a single store for data aggregated from across multiple source systems, and normalized to an industry standard canonical format - HL7 FHIR®. The artifact on which FHIR is settled are the 'resources', which contain any information related to clinical and administrative procedures. For the purposes of CTC application, the needed resources for structuring the information are: Media, a resource which can contain a photo, video or audio recording acquired or used in healthcare; Observation, a resource which can contain simple assertions, i.e., measures, made about a patient; DiagnosticReport, a resource which can contain the findings and interpretation of diagnostic tests performed on patients.

Given that the input of the CTC application is the set of layers of an image produced by a confocal microscopy unit, we need the Media resource (Figure 2). On the other hand, to store the number of CTCs detected by our AI module, an Observation resource is selected (Figure 1). Lastly, the DiagnosticReport is the appropriate resource to link both Media(s) and Observation(s).


```json
{
  "resourceType": "Observation",
  "id": "UKCM-CTC-36",
  "status": "final",
  "category": [
    {
      "coding": [
        {
          "system": "http://hl7.org/fhir/observation-category",
          "code": "laboratory",
          "display": "Laboratory"
        }
      ]
    }
  ],
  "code": {
    "coding": [
      {
        "system": "http://loinc.org",
        "code": "67568-6",
        "display": "Circulating tumor cells.breast [#/volume] in Blood"
      }
    ]
  },
  "subject": {
    "reference": "Patient/UKCM-CTC-81911"
  },
  "effectiveDateTime": "2013-05-15T19:32:52+01:00",
  "valueQuantity": {
    "value": 378,
    "unit": "lbs",
    "system": "http://unitsofmeasure.org",
    "code": "{cells}/uL"
  }
}
```


Figure 1– Example of CTC counting Observation.

As for codes and categories needed inside the FHIR resources, it is strongly advisable to use standardize terminology, such as LOINC or SNOMED. Whenever needed, FHIR also provides custom identifiers, for example, to classify Observations into different categories. Lastly, the DiagnosticReport resource may possess a code or name that helps to interpret the type information it contains. Given that at this stage only the general CTC counting will be address, but further information will be added, a custom identifier was created in the framework of PERSIST project: ‘ctc-panel’, flexible enough to capture all the expected data.


```
{
  "resourceType": "Media",
  "id": "UKCM-CTC-150033",
  "type": "photo",
  "subtype": {
    "coding": [
      {
        "system": "http://snomed.info/sct",
        "code": "60287000",
        "display": "Photography, microscopic"
      }
    ]
  },
  "subject": {
    "reference": "Patient/UKCM-CTC-81911"
  },
  "occurrenceDateTime": "2013-05-15T19:32:52+01:00",
  "content": {
    "data":
"R0lGODlhfgCRAPcAAAAAAIAAAACAAICAAAAAgIAAgACAgICAgMDAw
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAMwAAZgAAmQAAzAAA/wAzAAAzMwAzZgAzmQAzzAAz/wBmA
ZmQCZzACZ/wDMAADMMwDMZgDMmQDMzADM/wD/AAD/MwD/ZgD/mQD/z
Knaja4uHrtWEa4beqRZpJpXcvy3kaxhxD6U/NqaQ0xCr6jJhpFUlYP
SKVRAG955u3SJdhITZ766KosyNjQOnZAt6F3d7oQJ+inaJNPrHUXt"
  }
}
```


Figure 2– Example of Media storing one layer.


```
{
  "resourceType": "DiagnosticReport",
  "id": "UKCM-CTC-792739",
  "status": "final",
  "code": {
    "coding": [
      {
        "system": "http://projectpersist.eu/CodeSystem/ctc",
        "code": "ctc-panel",
        "display": "CTC panel"
      }
    ]
  },
  "subject": {
    "reference": "Patient/UKCM-CTC-81911"
  },
  "issued": "2013-05-15T19:32:52+01:00",
  "image": [
    {
      "link": {
        "reference": "Media/UKCM-CTC-150033"
      }
    },
    {
      "link": {
        "reference": "Media/UKCM-CTC-150034"
      }
    }
  ],
  "result": [
    {
      "reference": "Observation/UKCM-CTC-36"
    }
  ]
}
```


Figure 3– DiagnosticReport linking two layer (Media) and its Observation.

Results

In the present document we have showed the utility of CTC counting in cancer treatment and follow-up. Likewise, it was discussed the need of tools for an automatic counting of CTCs. In order to build an interoperable system, we have analyzed available open standards and international terminologies, finally choosing FHIR to structure the data and LOINC and SNOMED to encode the terms. Based on this selection, we performed a study to build the most appropriate resources and their codes, drafting customized ones when needed.

Conclusions

Through this work we describe how suitable are CTCs counting to detect cancer recurrence and metastasis. Likewise, we also analysed the feasibility of FHIR as a standard capable of storing liquid biopsy information.

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Address for correspondence

Victoria M. Cal González
email: vcal@gradiant.org
Lorena González Castro
email: lgonzalez@gradiant.org