

Title	Assessment of tissue or cell sample preparation, qualification and selection procedures for cancer somatic gene testing
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Aim

The objective of this work is to specify the usefulness, the indications and methods of tissue or cell sample preparation, qualification and selection in anatomical pathology, in view of cancers somatic genetic analysis.

Conclusions and results

Eight good practice guidelines, two of which French, four technical guidelines and two technical articles were selected to evaluate tissue or cell sample preparation, qualification and selection procedures for cancer somatic gene testing.

The method of development and the methodological quality of the good practice guidelines were analysed using the AGREE II check-list.

Most of the good practice guidelines analysed agree on the need to ensure anatomical pathology and genetic results are representative and consistent, by first making a fine selection of samples to be used prior to any cancer somatic gene testing.

In the literature analysed, no elements likely to bring preparation techniques into question were identified. These technical procedures are based on consensus and used historically. Observation of soft tissue after embedding in paraffin dates back to the mid-19th Century. Cryopreservation has been in use since 1954 and the use of microtomes dates from the end of the 18th Century.

Professionals fully adhere to the consensus which comes out of the analysis of the literature and confirm that any tissue somatic gene testing requires prior selection and preparation of the tissue sample.

On the conditions of preparation, qualification and selection of samples in view of cancer somatic gene testing, the stakeholders have cited or used the 2009 guidelines from the French National Authority for Health and the 2011 INCA guidelines which still apply today.

Indications

Fixation and embedding can be used in the following cases:

- Solid tumours:
 - brain tumours;
 - digestive tumours:
 - colorectal cancer;
 - gastro-intestinal stromal tumours (GIST);
 - stomach tumours;

- hereditary nonpolyposis colorectal cancer;
- lung carcinoma;
- breast cancer;
- melanoma.

In the absence of an alternative, other solid tumours and lymphomas can be fixed and embedded before genetic testing is carried out.

Cryopreservation can be used in all contexts of testing for genetic alterations, but it is not recommended to replace cryopreservation with fixation/embedding in the following cases:

- solid tumours and lymphomas:
 - sarcomas;
 - lymphomas;
 - paediatric tumours.
- leukaemia and other haemopathies (not including lymphomas):
 - AML;
 - ALL;
 - CLL;
 - CML;
 - non-CML myeloproliferative neoplasm;
 - multiple myeloma;
 - myelodysplastic syndrome.

For cryopreservation, part of the sample must be examined macroscopically and microscopically in order to qualify the sample, even if it is obvious that it is a more complex approach than for fixed tissue.

Issue of results

It is important for the results of these procedures to be formalised in a report stating:

- the patient's identification;
 - the description of the sample (sample type, site, laterality, number, and quality: size, presence of tumour and where applicable discordance between the type observed and the type expected);
 - the clinical context;
 - tumour cellularity;
 - the presence of any confounder (necrosis, cell type (stromal cells including immune cells), fibrosis etc.).
- Samples for the cancer somatic gene test are selected or the selection is validated after qualification.

With regard to these elements, the HAS considers that tissue or cell sample preparation, qualification and selection procedures in anatomical pathology (either paraffin fixation and embedding (with the procedure N005), or cryopreservation (with the procedure N006)) are required for the proper analysis of these samples in cancer somatic genetics.

Methods

The assessment method used in this report is based on the critical analysis of the data identified in the scientific literature and the recording of the justified opinion of healthcare professionals. A literature search was performed between January 2009 and March 2019, followed by watch up to December 2019. The stakeholders were consulted in September 2019.

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