# Artificial neural network a promising tool for the separation of reactive atypical mesothelial cells from malignant mesothelioma in pleural effusion cytology.

**G.Planchard[1], M.Lecluse[2], D.Matte[3], H.Elie[2], A.Elmoataz[3], O.Lézoray[3], F.Galateau-Sallé[1]**

[1]Department of Pathology, Centre Hospitalier Universitaire de Caen, Caen, France
[2]Department of Pathology, Centre Hospitalier Publique du Cotentin, Cherbourg-Octeville, France
[3]GREYC, UMR 6072, Université de Caen Basse-Normandie, Caen, France

## INTRODUCTION

The term “atypical mesothelial hyperplasia (AMH)” defines mesothelial cells with atypia suspicious for malignancy on cytology samples or pleural biopsy. It means, that on morphology alone, we don’t know, if the cells are reactive or malignant. This situation represents 22 to 47% of cases (1).
The 3-years survival of patients with a diagnosis of AMH is about 60% versus approximatively 15% for mesothelioma cases (Group Mesopath data). Currently, the presence of p16 deletion by FISH is a very promising marker for prediction of malignancy, but is not routinely available everywhere and moreover is not definitively recommended for individual diagnosis in the absence of strong clinical and radiological evidence of malignancy (2).
Other markers of malignancy have been studied: positivity of EMA, p53, GLUT-1, X-linked inhibitor of apoptosis, IMP-3 and negativity of desmine on immunohistochemistry (3), aneuploidy (4), high count of AgNORs (5), high optical density, textured and marginated chromatin on morphometry (6). But none are validated on individual diagnosis.

## AIM

To build an artificial neural network (ANN) model for the study of AMH and the detection of AMH that will progress to malignant mesothelioma (MM).

## MATERIALS AND METHODS

### Populations

We selected a total of 54 effusion cytology cases consisting of 18 MM, 18 benign cases and 18 AMH. Out of the 18 AMH, 9 have turned into MM and 9 remained benign after 2 years survival. The diagnosis of MM and AMH was validated on control pleural biopsies and were definitively certified by the MESOPATH group. Cytospin slides were Papanicolaou stained and scanned by the scanner Leica SCN400.

### Image Analysis System

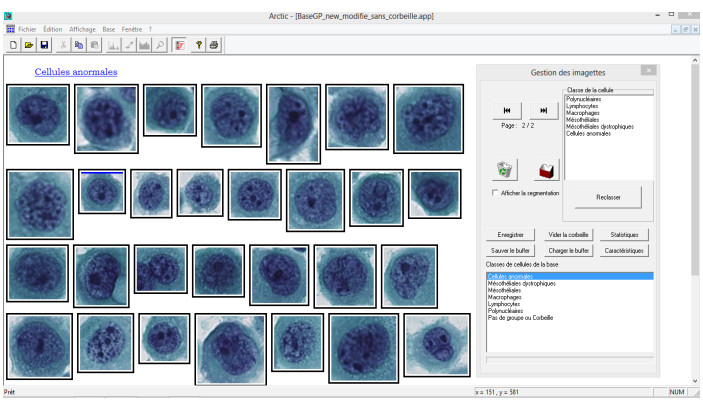
We used an experimental software named ARCTIC (*Aide en Cytologie par le Tri Informatisé des cellules*) which belong to Datexim company.
ARCTIC is a semi-automatic screening system. It is a diagnosis aid for detecting abnormal cells on Papanicolaou stained slide.
ARCTIC has already been succeed on serosal pathology with detection of 98,5% of malignant cases (VALTRICYT program) (7).
It is based on three sequential steps:

-**segmentation** of the nucleus

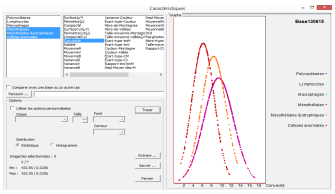
-**characterization** of the nucleus by the extracted morphometric and textural nuclear features (31 nuclear features are studied and divided in 5 categories: size, shape, color/grey scale, texture and spatial distribution of chromatin).

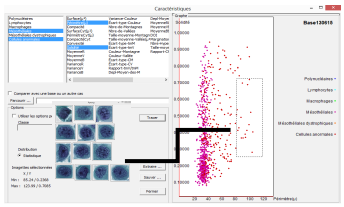
-**classification** of the cells by MONNA system (8) in 6 categories (abnormal cells [a], dystrophic mesothelial cells [b], benign mesothelial cells [c], macrophages, lymphocytes, leucocytes),

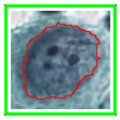
The cells are presented on galleries by categories. Thus, cells recognized as abnormal by ARCTIC can be checked easily by the pathologist. Finally, the pathologist will confirm or not the diagnosis of malignancy suggested by ARCTIC.



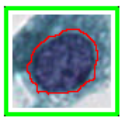

The system also allows the display and the comparison of the characteristics of a cells group as a Gaussian (one feature) or a scatter plot (two features).



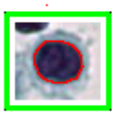




[a]



[b]



[c]

## RESULTS

Our ANN model has detected abnormal cells in 80% of MM and 62% of AMH which behaved as MM.

Nuclear size, nuclear shape, texture parameters and spatial repartition of chromatin were discriminant to separate malignant from benign mesothelial cells (fig 1).

Nuclear size, texture parameters and spatial repartition of the chromatin were decisive factors for the separation between AMH which behaved as MM and benign AMH (fig 2).

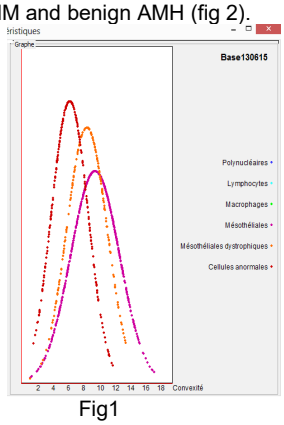



Fig1

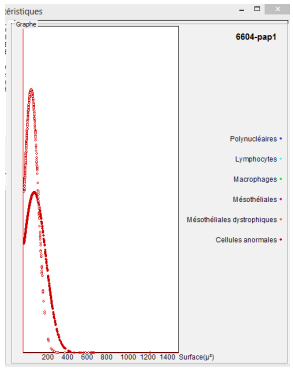



fig 2

## CONCLUSION

Our ANN model is a very promising tool for the detection of malignant mesothelial cells on routine pleural effusion cytology.
Nowaday, it is not enough powerful to detect AMH that will progress to malignant mesothelioma (MM) even if we show morphometrics differences between benign AMH and AMH which behaved as MM.
Larger studies are needed to validate this technology.

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