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LEVERAGING RANDOM SURVIVAL FOREST (RSF) AND PET IMAGES FOR PROGNOSIS OF MULTIPLE MYELOMA AT DIAGNOSIS

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Context

Multiple myeloma (MM) is a bone marrow cancer that accounts for 10% of all haematological malignancies. It was reported that **full-body FDG PET imaging** provides prognostic information for both baseline and therapeutic follow-up of MM patients (MM).

Aims

- ✓ Predict Progression-Free Survival (PFS).
- ✓ Provide predictive features (Clinics and Radiomics).

Contribution

There is yet much to discover in the survival analysis of MM. However, the **Random Survival Forest (RSF)**[2] has demonstrated robustness but is not studied in the PET imaging and MM context. We developed a two-stage computer-assisted method based on PET imaging features towards **assisting current diagnosis and treatment decisions** for MM patients, with RSF and **"Variable importance" (VIMP)** [2].

Definitions

Right censoring: When no event (death/relapse) has taken place at the end of the evaluation period.

C-index: The concordance probability is the frequency of concordant pairs among all pairs of subjects.
 $Error\ prediction = 1 - C-index$

Survival curve: Survival rates of a specific population, over a period of time.

A. Material and method

1) The data

- ✓ Prospective multi-centric french IMAJEM study [1], 66 patients
- ✓ 132 Clinical and imaging features (textural and conventional).

2) The textural features : Radiomics

Example of the GLCM (Gray-Level Co-Occurrence) Matrix [3]:

Translate the joint probability $P(i,j|\sigma,\theta)$ of the ROI. The position (i,j) represents the number of times that the **combination of the pixels with i and j levels** appears in the I matrix, separated by σ **pixels distance** and a θ **angle**.

For a distance of 1 and an angle of 0° (plan horizontal):

1	2	5	2	3
3	2	1	3	1
1	3	5	5	2
1	1	1	1	2
1	2	4	3	5

Fig. 2: Intensity matrix I

6	4	3	0	0
4	0	2	1	3
3	2	0	1	2
0	1	1	0	0
0	3	2	0	2

Fig. 3: GLCM Matrix p

$$Energy = \sum_{i=1}^{Np} \sum_{j=1}^{Np} (p(i,j))^2 \quad (1)$$

with $Np * Np$ the size of the GLCM matrix



Fig. 1: FDG-PET image of a multiple myeloma patient

3) The method

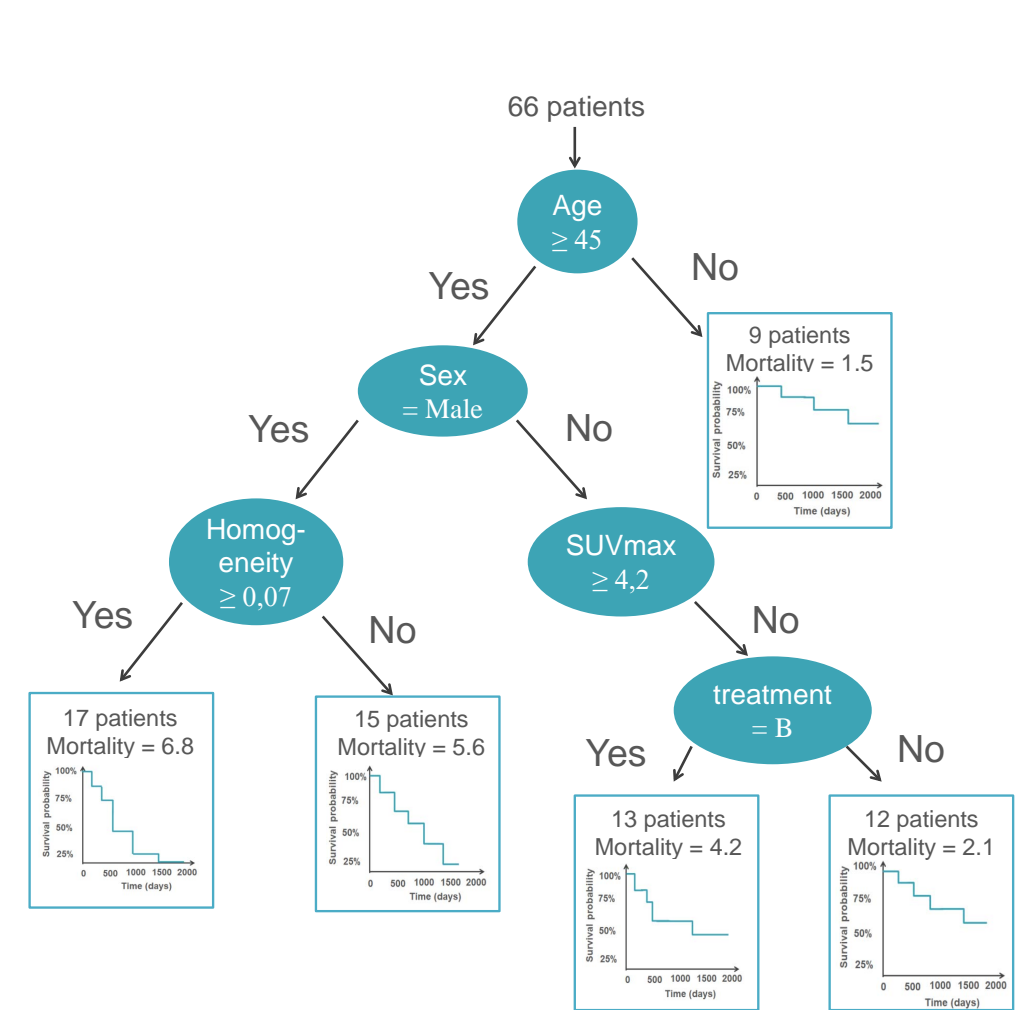


Fig. 4: The RSF differs from the random forest in the target value (the ensemble mortality) but also in the way to separate branches (log-rank test on the mortality)

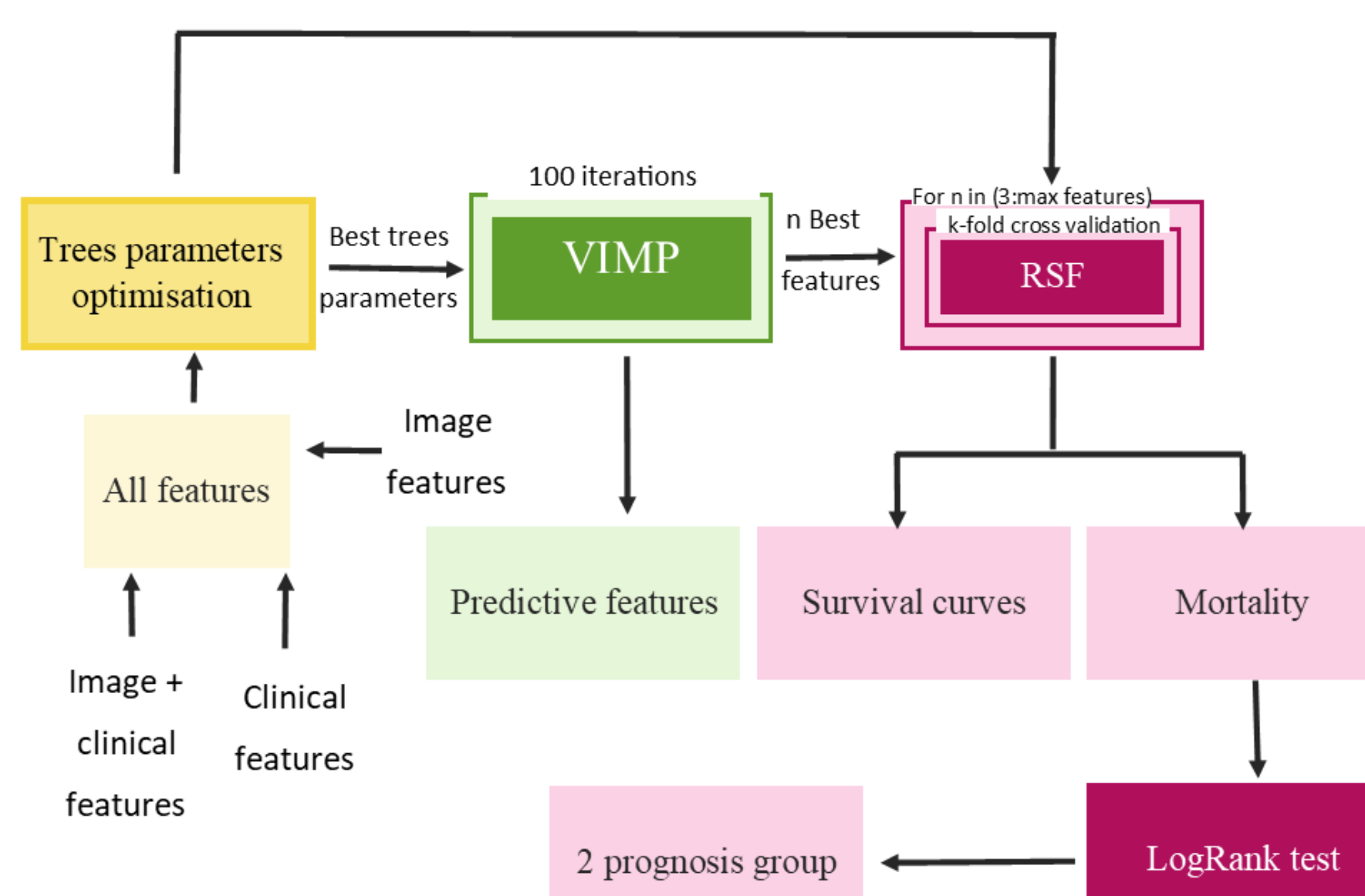


Fig. 5: pipeline of the method

B. Results

1) Evaluation of the method

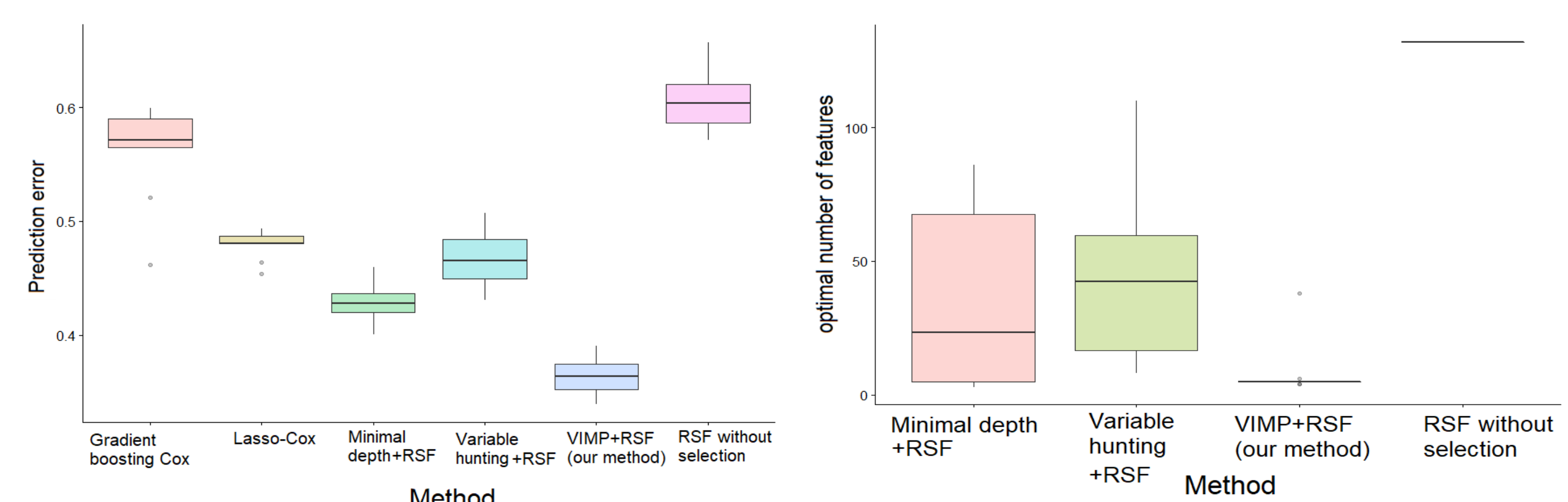


Fig. 6: Prediction error for each method.

Fig. 7: Optimal number of features kept per method.

Method	Average p-value
Our method	0.05
Gradient-Boosting Cox	0.27
Lasso-Cox	0.4
Without selection	0.40
Minimal depth	0.24
Variable-Hunting	0.11

Tab. 1: Average p-value according to the method.

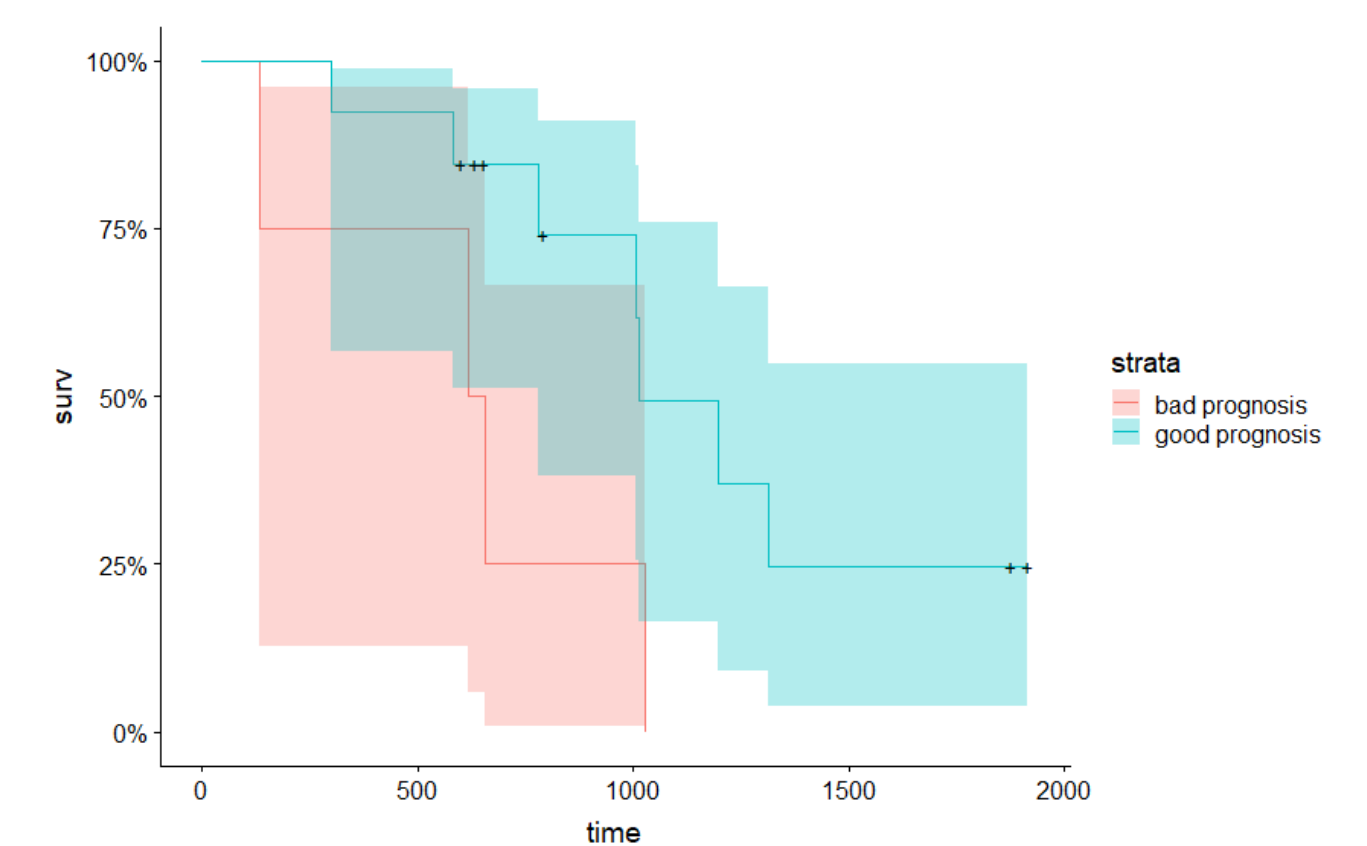


Fig. 8: Kaplan Meier curves of the two groups obtained with the test set (pink : bad prognosis, blue : good prognosis). Error : 0.39, p-value = 0.045

3) The interest of using textural features

	All characteristics	textural and conventional characteristics	clinical characteristics
Our method	0.34	0.36	0.45
Minimal depth method	0.45	0.45	0.48
Variable-Hunting method	0.40	0.41	0.45
Without selection	0.51	0.67	0.52

Tab.2: Influence of the features class on the prediction error, with different selection methods. There are the same patients in each sub-databases

3) The predictive features

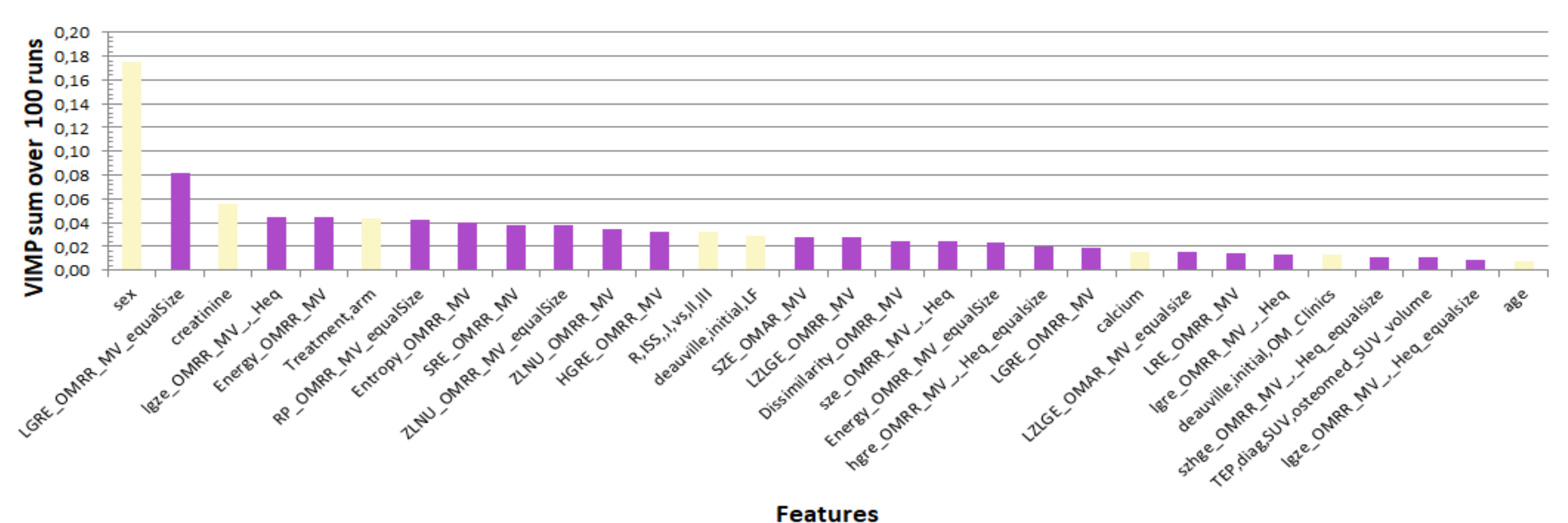


Fig. 8 : Histogram of the features found as predictive with the VIMP method. Yellow: clinical, purple: Imaging. OMRR (One Matrix relative resampling), OMAR (absolute resampling), Heq (histogram equalization), equalsize (equal size of voxels)

C. Conclusions and perspectives

- ✓ The proposed method is more efficient than conventional approaches.
- ✓ It is possible to correctly separate two classes of patients (good/bad prognosis).
- ✓ It is possible to determine the features that are the most predictive.
- ✓ It shows the interest of using textural features.
- ✓ The relative resampling is more predictive than absolute resampling
- ✓ This approach can be generalised to other diseases.
- ✓ Thereafter, more patients will be included.

References

- [1] P. Moreau, et al., Prospective evaluation of magnetic resonance imaging and [18f] fluorodeoxyglucose positron emission tomography-computed tomography at diagnosis and before maintenance therapy in symptomatic patients with multiple myeloma included in the ifm/dfci 2009 trial : Results of the imajem study. Journal of Clinical Oncology, 35(25).
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