

## Introduction

IDH1/2 mutations are indicative of good prognosis upon treatment and they may have intraoperative importance for disease management. Intraoperative diagnosis became a new technical approach in glioma management. If a neurosurgeon would know the mutation status in IDH genes, he/she would change the extent of resection in tumor removal. Because mutated tumors responsive to chemo/radiotherapy.

We aimed to conduct a comprehensive IDH mutation analysis by using PCR based methodology during surgery. Our aim is to provide rapid, highly sensitive and specific intraoperative mutation detection system with robust accuracy.

## Methods

Amplification refractory mutation system (ARMS) was modified and optimized. The novelty of our methodology is adding an extra mismatch to increase specificity. ARMS was used to detect the presence of all common IDH1 and IDH2 mutations including, R132H/C/S/G and R172K/M/W mutations in 236 glioma sample selected from our tumor bank and obtained prospectively. All results were also evaluated by Sanger sequencing and immunohistochemistry (IHC). We also evaluated the diagnostic and screening potential of the test by comparing the methods.

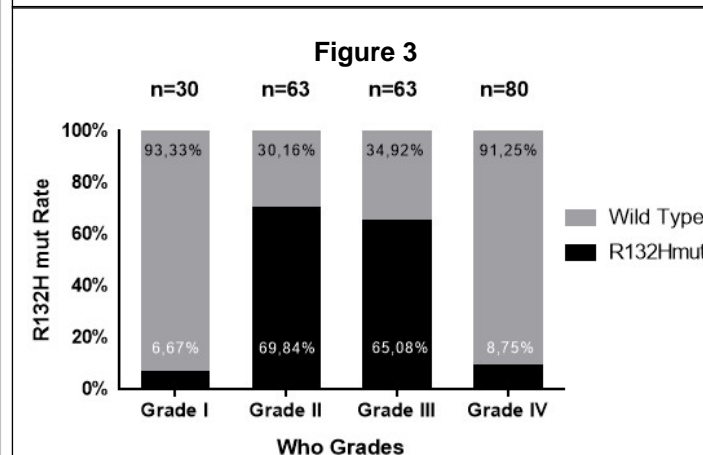
Figure 1

## Results

By addition of the third mismatch to conventional ARMS we successfully detect IDH1 and IDH2 mutations by 100% coherency with Sanger sequencing. Comparison between IHC and 3 mismatch-ARMS showed, 3-mismatch ARMS is superior to IHC in terms of accuracy, sensitive and specificity. Based on our results, frequencies of IDH1/2 mutations among different glioma grades are, 6.67%, 69.84%, 65.08% and %8.75 for grade I, II, III and IV respectively.



Agarose gel image of wtDNA and mutant DNA. Confirmation of results with real time qPCR and Sanger sequencing



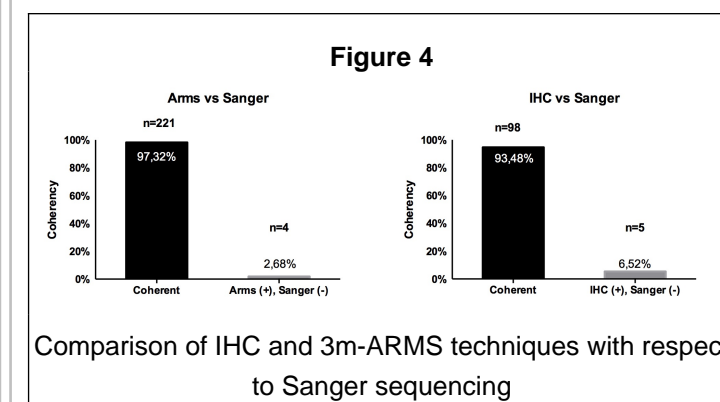
Distribution of mutation among different grade gliomas

## Conclusions

3-mismatch ARMS is a novel methodology with great potential to be used as a intra-operative diagnostic test. It can detect IDH mutations almost one hour without the need of sequencing with the ability to be adapted for detection of various mutations through easy primer design.

## Learning Objectives

By the conclusion of this session, participants should be able to: 1) Describe the importance of intraoperative diagnosis in glial tumors, 2) Discuss, the availability of PCR based methodological approaches in intra-operative diagnosis 3) Identify 3 mismatched ARMS method as novel suitable method in glial tumor molecular diagnosis



Comparison of IHC and 3m-ARMS techniques with respect to Sanger sequencing