



# Exploring the Use of a Restoration Step to Detect Mosaic Chromosomal Alterations in Prostate Samples

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## Introduction

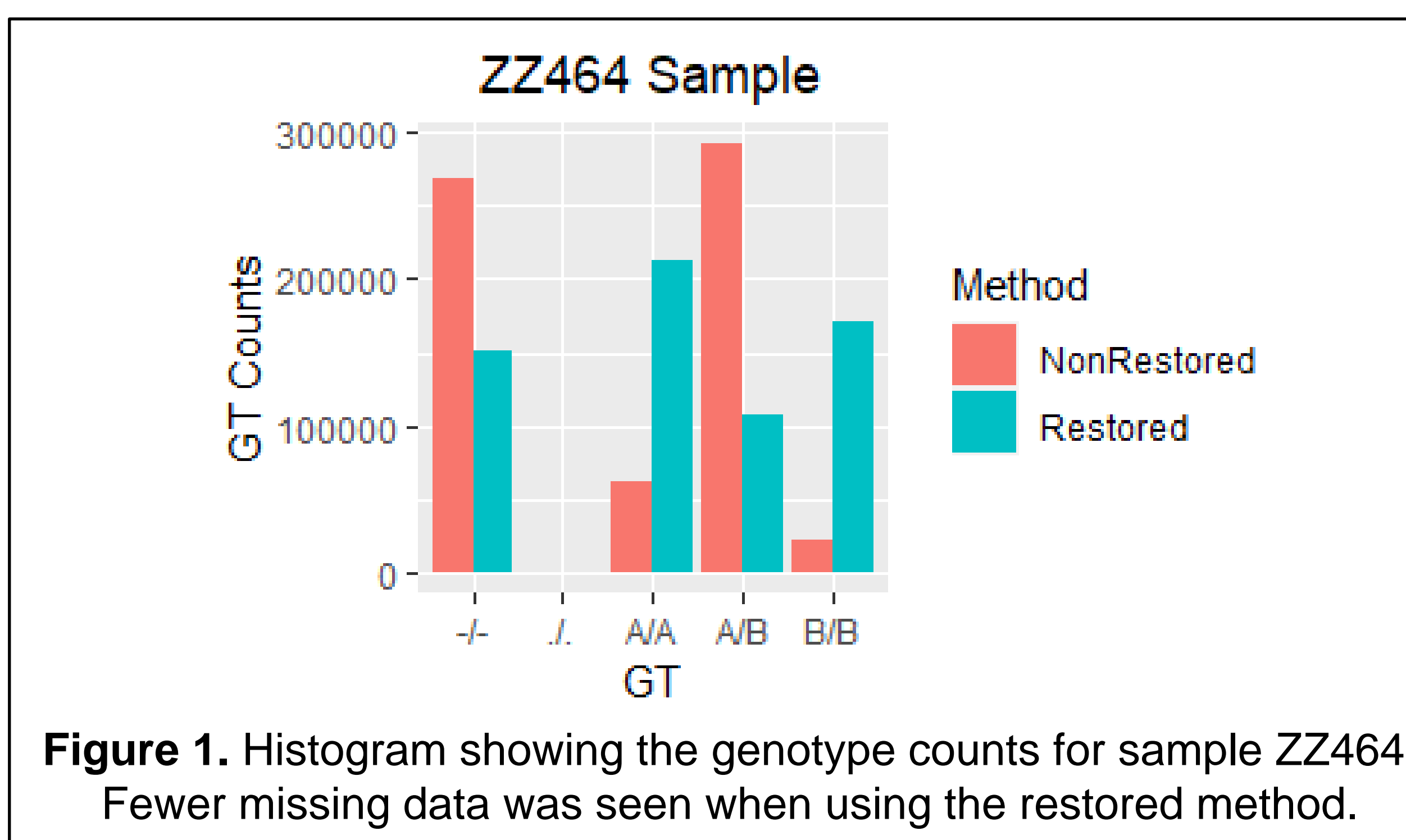
- Genetic instability is a hallmark in tumor prevalence, resulting in aneuploidy and copy-neutral loss of heterozygosity (cn-LOH) events.<sup>1</sup>
- The samples used in this pilot study were stored in formalin-fixed and paraffin-embedded (FFPE). Use of FFPE involves cross-linking, which causes DNA damage.<sup>2</sup>
- In addition, normal cell contamination and degradation in nucleic acid can make it difficult to identify mutations within a tumor sample due to dilution of the signal within the cells.<sup>1</sup>
- The hapLOH method was developed to assist in the detection of copy-number events. When adding the restoration step, the DNA concentration is further reduced.

## Materials and Methods

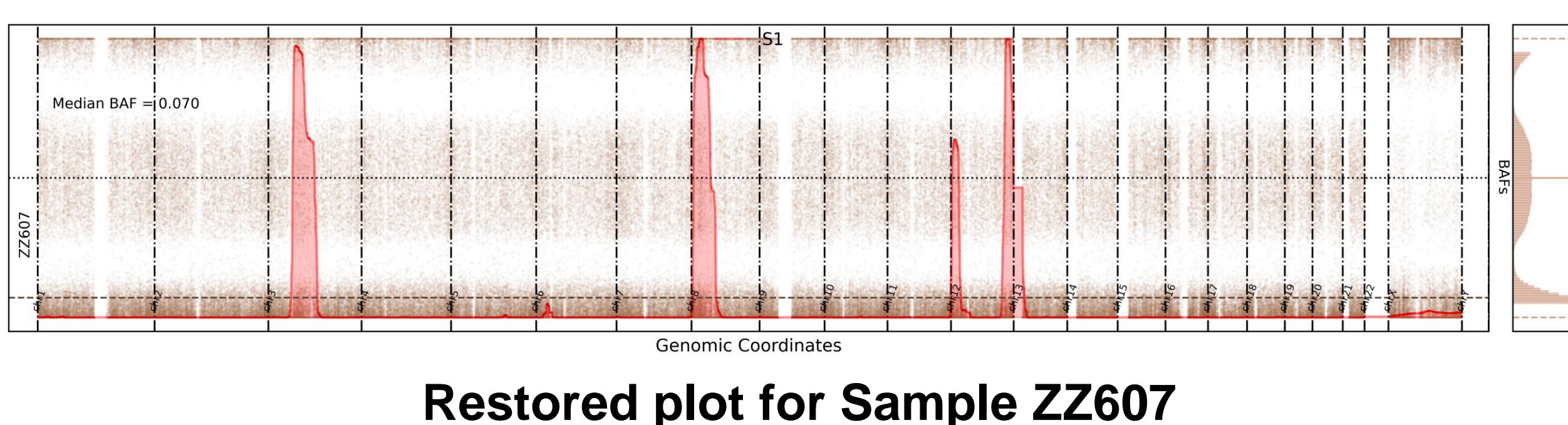
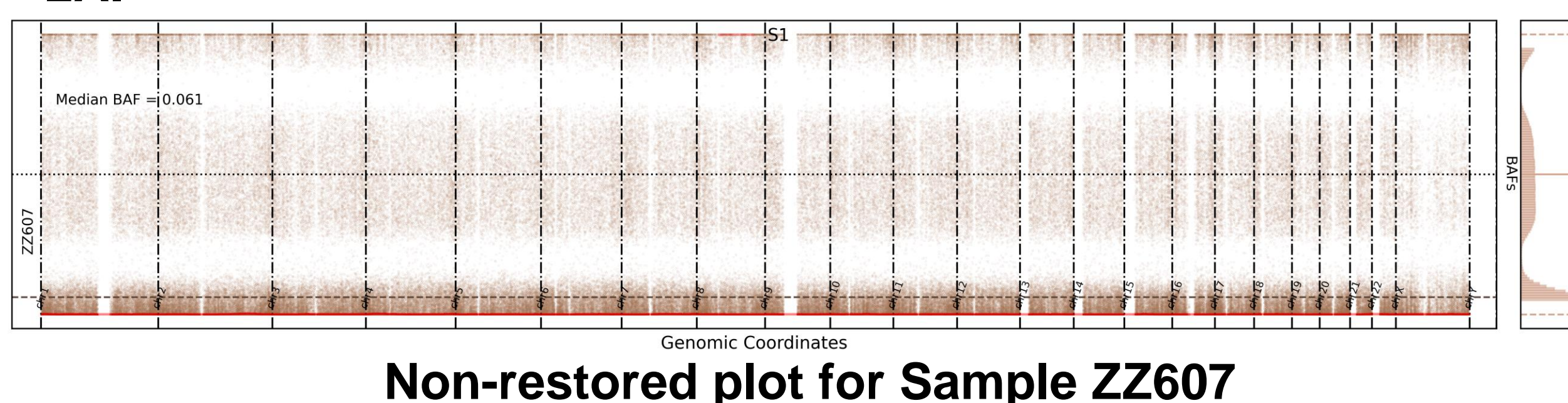
- The hapLOH method was used to determine the occurrence of subtle allelic imbalance (AI) in prostate samples.
- The best methodology (non-restored vs. restored) was determined.
- 24 samples were run twice -- with/without restoration -- for a total of 48 samples.
- Analyzed distribution of call rates and the specific genotype calls at single nucleotide polymorphisms (SNPs) between restored vs non-restored.

## Results

Histograms and hapLOH plots were analyzed for the 24 paired samples. Figures 1 and 2 show examples of the analyses that was conducted for two of the patients.



2A.



2B.



**Figure 2A.** hapLOH plots for the non-restored and restored methods for sample ZZ607. A greater number of mCAs were detected using the restored method.

**Figure 2B.** Histogram showing the genotype counts for sample ZZ607. Fewer missing data was seen when using the restored method.

## Results (Continued)

	Non-restored	Restored
<b>Number of Detected mCAs</b>	40	53

**Table 1.** A greater number of mosaic chromosomal alterations (mCAs) were detected when undergoing the restoration step.

## Conclusions

The restored method was determined to be the best and most accurate method because:

- It uses a modest amount of DNA, while detecting approximately 14 percent more mCAs.
- It yielded fewer missing data.

A drawback of the restored method is that it is three times more costly for the specific array used here.

## Future Directions

- The study team plans to conduct a much larger study.
- The large-scale study will include approximately 1,000 patients with advanced prostate cancer and 1,000 patients without advanced prostate cancer.

## References

- Vattathil, S., & Scheet, P. (2013). Haplotype-based profiling of subtle allelic imbalance with SNP arrays. *Genome research*, 23(1), 152–158. <https://doi.org/10.1101/gr.141374.112>.
- Klages-Mundt, N. L., & Li, L. (2017). Formation and repair of DNA-protein crosslink damage. *Science China. Life sciences*, 60(10), 1065–1076. <https://doi.org/10.1007/s11427-017-9183-4>