





**Figure 2. Standard Curve for 20 mer Oligonucleotide.** Good linearity was obtained from 1.75 fmol to 2 pmol oligo nucleotide on spot. The lower limit of quantitation (LLOQ) obtained was 1.75 fmol showing good sensitivity for this application by MALDI TOF analysis.

## Results

Figure 1 shows both the analyte (20mer) and the internal standard (22mer) can be easily detected with high resolution ( $R \approx 20000$ ). Shahgholi et al.1 reported various sugars can be used as matrix additives to enhance the sample uniformity and minimize the transfer of excess laser energy to oligonucleotides. As a result, a higher laser power can be used to ensure the generation of enough ions for quantitation without compromising the data quality.

To get the best reproducibility and minimize the effect of “hot spots”, an internal standard is still necessary. In this experiment, the average peak area of the 22mer standard was used to normalize the peak area of the analytes at every concentration level. Five replicates were acquired for the analytes at each concentration level. The average normalized peak area at each concentration level was used for plotting the standard curve. The standard deviation within the same concentration is less than 18%. As shown in Figure 2, good linearity across 3 orders of dynamic range was achieved, with  $r$  value of 0.99 and the lower limit of quantitation at low fmol level.

## Conclusions

The 4800 Plus MALDI TOF/TOF™ Analyzer is a robust platform for analyzing oligonucleotides. By using internal standards and matrix additives, good linearity can be achieved within 3 orders of magnitude.

## References

1. Mona Shahgholi, Benjamin A. Garcia, Norman H. L. Chiu, Paul J. Heaney and Kai Tang, *Nuclei Acids Research*, 2001, Vol. 29, No. 19.

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