Multiple myeloma is a cancer of the plasma cell characterized by overproduction of monoclonal immunoglobulins, renal damage, and cytologic lesions as a complication of diffuse osteoporosis. Although there is currently no cure, there are specific cytogenetic and FISH abnormalities that help determine the course of the disease. Advances in the field of cell separation have led to plasma cell enrichment (PCE), which isolates the cells of cancerous origin. This enriched sample can then be analyzed with higher specificity. The purpose of this study was to compare automated and manual methods of PCE as a function of abnormality detection and cost. Is the higher capital investment for an automated PCE instrument justified? Our investigation supports the use of PCE automation to better enrich samples, detect abnormalities, and increase efficiency allowing technologists time to perform other tasks in the laboratory.

INTRODUCTION

Multiple myeloma is a malignant plasma cell neoplasm characterized by overproduction of monoclonal immunoglobulins, hypercalcemia, anemia, and renal damage, as well as diffuse osteoporosis with advancement to solitary lesions.1 There are other plasma cell neoplasms closely related to myeloma, which include monoclonal gammopathy of undetermined significance (MGUS), and monoclonal gammopathies associated with plasma cell disorders (PCP).2,3

METHODS

Automated Plasma Cell Enrichment

Bone marrow specimens were received in heparinized red blood cell lysing solution and were separated into a 5% dimethylsulfoxide (DMSO) acid ethanol (AE) acid solution, the specimen volume and quality. Mixtures of at least 90% of the plasma cells were then eluted into centrifuge tubes and a subsequent direct harvest was performed. The fixed cells were dropped and probed the same day using class 1/2 Analytic Specific Reagents (65%) for chromosome 13 deletions, deletions of 17p, IGH/MCF11 (1/4-16), IGHSF/CCND1 (4/14), and IGHSF/BCI (11/14). These probes are locus-specific probes.

Automated Costs

The fixed cells were dropped and probed the same day using class 1 Analytic Specific Reagents (65%) for chromosome 13 deletions, deletions of 17p, IGH/MCF11 (1/4-16), IGHSF/CCND1 (4/14), and IGHSF/BCI (11/14). These probes are locus-specific probes.

RESULTS

The side-by-side study showed a 23% increase in the overall abnormality detection among probe sets using the automated approach. Included in the count were four assays in which an abnormality was detected using the automated method, but not using manual PCE. The opposite was not found. Figure 1 illustrates the results of the probe set with chromosome 13 and 17p deletions. The automated procedure identified 8% more abnormalities from the patient samples that underwent automated plasma cell enrichment at a distribution of 76%, compared to 68% of the abnormalities detected from manually enriched samples. For the automated method, there were twice as many patient samples with low cellularity.

The cost analysis revealed an annualized savings of $91,072 by utilizing the Auto-MACS machine (Figure 3). The reusable separation columns and the reduction of technician time factor in to reduce the majority of the cost. The payback period of the initial capital investment was determined to be 5.16 years.

DISCUSSION

By evaluating the side-by-side study, it becomes evident that using the automated approach to plasma cell enrichment does indeed increase the rate of interphase FISH abnormality detection. This indicates a more authentic population of plasma cells isolated using automated PCE. The large proportion of patients with t(11;14) abnormalities coincides with findings from previous studies, as this abnormality has been associated with all three disease stages of plasma cell neoplasms.4 Although direct comparisons cannot be made between the sixty patient samples analyzed using manual PCE and those by the automated method, correlations can be made in terms of the distribution of signal abnormalities. The most prevalent abnormalities were associated with a 13q deletion, which is consistent with findings in previous studies. However, the incidence of 13q deletions in all three disease stages of plasma cell neoplasms has not been addressed. We also observed an abnormality resulting in a fusion gene of chromosome 13q deletions, deletions of 17p, IGH/MCF11 (1/4-16), IGHSF/CCND1 (4/14), and IGHSF/BCI (11/14). These probes are locus-specific probes.

CONCLUSION

Our investigation supports the use of PCE automation to better enrich samples, detect abnormalities, save money as well as provide more time for the technologists to do other tasks. However, these studies are indicated indicating analysis of the limitations of the plasma cell population within the marrow sample, confirmation of plasma cell purity through cell sorting and counting techniques, comparing the effect of different anticoagulants on plasma cell enrichment, and the effect of sample volume or quality on the enriched plasma cell suspension. Although there is much to explore in the field of automated plasma cell enrichment, it is clear that the enrichment of plasma cells to detect interphase FISH abnormalities is warranted. As more is learned about this field, implications for automated testing will also increase.

ACKNOWLEDGMENT

Thank you to Sue Ellen Sexton for her contributions on the cost analysis.