Conclusion
Part VII: CONCLUSION

Applications of the results in disease management and future prospects for research.

In India over 70-80% of cancer patients, report to hospitals with stage III or IV disease. Management of disease becomes more complicated in such advanced stages (Lippman et al., 1989). Need for predicting risk multiple recurrence of tumor is the subject of serious concern (Franco, 1991). To date there are no specific biological criteria to pre-determine the efficiency of the proposed treatment. Further treatment failure is more often as a result of biological resistance. Results from previous research for prognostic markers remain controversial (Cheisa et al., 1999). This is because there are no specific criteria (such as range of values or fixed values or percentage of expression of a marker etc.,) to demarcate high-risk groups from low-risk groups. Such a rational approach is needed for designing and planning treatment modalities. Studies on optimizing treatment modalities report, that there is no such rational available and expresses concern on the need of such rational (Kirita et al., 1999). An extensive survey on 2000 papers published, in past 5 years indicate that various prognostic markers are available. However to use such markers in routine practice remains controversial (Chiesa et al, 1999).

This study selected oral cancer as the model. Oral cancer is a common malignancy in India and its biological behaviour is often highly variable. Biological markers analyzed in various other cancers can also be applicable for oral cancer. Therefore predictive assays developed based on the results obtained from the present study may be extended for other cancers too. This is so, because angiogenesis, proliferation and apoptosis are common phenomena involved in many tumors. Most molecular factors associated with tumorigenesis in-turn
reflect their function(s) in any of these three parameters. Therefore such a novel approach based functional relations can serve as an ideal model for other cancers.

Such a novel predictive assay reported in this study may find potential application with treatment advances such as 3D stereotactic radiotherapy, radiolabeled immunoglobulins and hypoxic radiosensitizers. Trials on estimating the radiation dose necessary to control a specific tumor volume are currently being investigated, Willner et al., (1999) reported encouraging results on the efficiency of 3D radiotherapy for nasopharyngeal carcinoma. Further, advances in computer software and image analysis show access to a 3D visualization at each step of the design and verification of a plan allowing to simulate the beams' irradiation effects on tumors as well as healthy tissues in terms of delivered radiation doses and also finally to assess the validity of a beam setup. (Robineau et al., 2000). The predictive assay designed in this study might find potential applications aiding in design and plan treatment trials with these advanced forms of therapeutic approaches.

This study has further scope for basic research including analysis for differential regulation of apoptosis in tumor cells, influence of host factors, whether the angiogenic phenotypes can further be classified as an ‘apoptotic sensitive’-angiogenic phenotype and a ‘apoptotic resistant’ angiogenic phenotype ?, whether switching on to angiogenic phenotype is associated with switching off apoptosis ?, etc., Such studies have also relevance in developing newer drugs.
A rationale for the use of multiple anti-angiogenic agents as a means of developing new chemopreventive protocols that result in reduced patient toxicity while maintaining similar clinical efficacies in controlling relapses in head and neck cancers has been described by (Lingen MW. 1999.)

The results from various clinical trials with newer anticancer drugs described by Buolamwini JK., (1999) also implicate angiogenesis, apoptosis and proliferation as major targets. In addition, blocking of the expression of drug resistance proteins, bcl-2 protein, MDM-2, Survivin and telomerase are being currently explored. Therefore extensive applications are possible with the predictive assay described in this study.

The objective of designing a predictive assay was achieved in the present study. Further applications and extension of this work should prove the significance of results obtained from this study.

To conclude, analysis for apoptosis and proliferation around the vascular area provides vital clues for predicting treatment response, while analysis for presence of mutant p53 protein, over-expression of bcl-2 protein etc., provides additional information on treatment resistance.