Laporan Akhir
IRPA Jangka Pendek

DR. BISWA MOHAN BISWAL

Semua laporan kemajuan dan laporan akhir yang dikemukakan kepada Bahagian Penyelidikan dan Pembangunan perlu terlebih dahulu disampaikan untuk penelitian dan perakuan Jawatankuasa Penyelidikan di pusat pengajian

USM R&D/JP-04

LAPORAN AKHIR PROJEK PENYELIDIKAN

R & D JANGKA PENDEK

A. MAKLUMAT AM

Tajuk Projek: Usefulness of Nuclear Morphometry and AgNOR score in predicting Radiation Response in squamous cell cancer of head and neck.

Tajuk Program: IRPA short term Grant 391/9039/1039

Tarikh Mula: 1st November 1998

Nama Penyelidik Utama: Dr Biswa Mohan Biswal
(*berserta No. K/P*) S-228973

Nama Penyelidik Lain: Dr Nor Hayati Othman
(*berserta No. K/P*) 4666881

B. PENCAPAIAN PROJEK:

(Sila tandakan / pada kotak yang bersesuaian dan terangkan secara ringkas di dalam ruang di bawah ini. Sekiranya perlu, sila gunakan kertas yang berasingan).

☐ **Penemuan asli/peningkatan pengetahuan**

We used argyrophilic nuclear organizer region (AgNOR) score, and nuclear Morphometry to predict radiation response in head & neck cancers. In this research, we found a correlation between nuclear Morphometry and response to radiation.

☐ **Rekaan atau perkembangan produk baru,**
(*Sila beri penjelasan/makluman agar mudah dikomputerkan*).

(1) We found a correlation between AgNOR score and Nuclear morphometry

(2) and ~~predict~~ radiation Response.

(3)

☐ **Mengembangkan proses atau teknik baru,**
(*Sila beri penjelasan/makluman agar mudah dikomputerkan*).

(1) Use of Nuclear measurement to predict Radiation Response is a new technique.

(2) In future this te

(3)

☐ **Memperbaiki/meningkatkan produk/proses/teknik yang sedia ada.**
(*Sila beri penjelasan/makluman agar mudah dikomputerkan*).

(1) The above research could have been further improved by using newer computer

(2) imaging technique to determine nuclear Roundness factor (NRF) By ~~requiring more number of subjects~~ in the study.

(3)

C. PEMINDAHAN TEKNOLOGI

☐ **Berjaya memindahkan teknologi.**

Nama Klien: *(Nyatakan nama penerima pemindahan teknologi ini dan sama ada daripada pihak swasta ataupun sektor awam)*

(1) Nuclear morphometry from FNAC slides can predict radiation Response in Head & Neck cancer.

(2) AgNOR score too can ~~predi~~ corroborate to predict radiation Response.

(3) .....

☐ **Berpotensi untuk pemindahan teknologi.**
(Nyatakan jenis klien yang mungkin berminat).

This technique will be helpful to Oncologists and Pathologists involved in the multidisciplinary Management of cancer.

D. KOMERSIALISASI

☐ **Berjaya dikomersialkan.** It is in preliminary stage to use this technique for commercialization.

Nama Klien: (1) .....

(2) .....

(3) .....

☐ **Berpotensi untuk dikomersialkan.**
(Nyatakan jenis klien yang mungkin berminat).

NA

E. **PERKHIDMATAN PERUNDINGAN BERBANGKIT DARIPADA PROJEK** (*Klien dan jenis perundingan*)

(1) NO

(2) .....

(3) .....

(4) .....

F. **PATEN/SIJIL INOVASI UTILITI**
(*Nyatakan nombor dan tarikh pendaftaran paten. Sekiranya paten/sijil inovasi utiliti telah dipohon tetapi masih belum didaftarkan, sila berikan nombor dan tarikh fail paten*).

(1) NO

(2) .....

(3) .....

G. **PENERBITAN HASIL DARIPADA PROJEK**

(i) **LAPORAN/KERTAS PERSIDANGAN ATAU SEMINAR**

(1) Part of the Research will be presented in coming NCMS 2000.

(2) Manuscript is already prepared for publication.

(3) .....

(4) .....

(5) .....

(ii) **PENERBITAN SAINTIFIK**

(1) Manuscript in the process of publication.

(2) .....

(3) .....

(4) .....

(5) .....

(6) .....

(7) .....

H. **HUBUNGAN DENGAN PENYELIDIK LAIN**
(Sama ada dengan institusi tempatan ataupun di luar negara)

(1) NIL

(2) .....

(3) .....

(4) .....

I. SUMBANGAN KEWANGAN DARI PIHAK LUAR
(Nyatakan nama ajensi dan nilai atau peralatan yang telah diberi).

NIL

(1) .....

(2) .....

(3) .....

J. PELAJAR IJAZAH LANJUTAN
(Nyatakan jumlah yang telah dilatih di dalam bidang berkaitan dan sama ada di peringkat sarjana atau Ph.D).

NIL

	Nama Pelajar
Sarjana	.....
	.....
	.....
Ph.D	.....
	.....
	.....

K. MAKLUMAT LAIN YANG BERKAITAN

As Nuclear morphometric technique to predict radiation response is new to our pathology department we had some difficulty at the begining. Hence we could not be able to do ~~in all~~ Nuclear morphometry in all cases. However, with our experience & this technique and encouraging correlation, we may like to use this technique in other cancer to predict therapeutic outcome.

29 March 2000
Tarikh

Tandatangan

T/TANGAN PENGERUSI
J/K PENYELIDIKAN
PUSAT PENGAJIAN

Usefulness of Nuclear Morphometry and AgNOR score in predicting radiation response in squamous cell cancer of the head and neck.

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Abstract

Squamous cell cancers of the head and neck have diverse biological behavior and prediction of radiation response. There is lack of specific investigation tool to predict the subgroup of cancers unresponsive to radiotherapy. This is a prospective study in the use of nuclear and nucleolar morphometric parameters for the prediction of radiation response. Twenty six patients with squamous cell cancers of the head and neck region were recruited to receive a course of palliative radiation therapy to a dose of 30Gy in 10 fractions over 2 weeks. Fine needle aspiration cytology was performed on day1 and day-5 of the above radiotherapy schedule. The AgNOR score and nuclear morphometric study was done using computerized image analyzer. A total of 26 patients were evaluable with a median age of 44 years (range 17-76 years). The primary tumors were from nasopharynx (11), larynx & hypopharynx (5), metastatic node (4), and miscellaneous tumors of head and neck (6). The response to radiation was gradual with a median regression time of 4 weeks. The mean AgNOR score was 3 dots/ nucleus (range (1.2-7 dots/nucleus). The average nuclear diameter was 11.073 μm (range 7.70-16.6 μm) and nucleolar diameter 2.92 μm (1.09-11.66 μm). Patients with higher pretreatment AgNOR score (> 2.5) were associated with disease progression and metastasis. However patients whose cancer cells showed increase in the diameter of the nucleus after initial radiotherapy fared better with local control by radiotherapy than those cancer cells were not.

Key words: radiotherapy, radiation response, nuclear morphometry, AgNOR

Introduction

Head and neck cancers are common malignancies among males, which accounts for 20% of all cancers (Parkin et al 1999). The malignancies have diverse biological behavior and prediction for disease progression. Surgery, radiotherapy and occasionally chemotherapy are the main modalities of treatment. Radiotherapy especially is being utilized among 60% of cancers either in the form of radical, adjuvant or in palliative intent. Not all patients who are given radiotherapy respond favourably. The common mode of radiotherapy treatment failure are manifested as residual disease, recurrent disease, and/or disease progression during treatment. Even cancer in the same histologic subgroups did not show uniform radiosensitiveness (Million and Cassissi 1984). Hence there are variation in the response to radiation therapy even when the other parameters like stage, site, tumor volume and histology are kept constant (Begg 1998). Histopathological subcategorizations too have not shown consistent predictor of response to radiotherapy (Meyer and Wang 1971). One approach to predict radiosensitivity is in the determination of response by in vivo tests like tumor cell culture and cell surviving fraction at 2 Gy dose of radiation (SF2) and the calculation of mean lethal dose (West et al 1993). Other methods are radiation induced histomorphological changes especially changes seen in the nucleus as a marker of radiosensitivity.

This concept of predicting radiosensitivity was firstly introduced by Graham in 1947 as the radiation response test (Graham 1947). Serial cytology slides were studied in the past to study the radiosensitivity of various cancers. Multinucleation and nuclear enlargement

of the malignant cells are common changes encountered following radiotherapy. Past radiobiological studies have shown that induction of multinucleated cells are dose related and correlated with cell survival assay, suggesting that they are non clonogenic (Bettega et al 1980). Radiation can induce fragmentation of the chromosome or form abnormal chromosomes which do not take part in mitosis. These chromosomal fragments are called micronuclei. Their induction are dose-related and correlated with survival (Grote et al 1981and Midander et al 1980).

Microscopically it is possible to observe the nuclear and nucleolar morphometry using computer assisted image analyzer (McLean et al 1996). These nucleolar events can be demonstrated by silver staining of the nuclear organizer region (AgNOR). The increase in the AgNOR counts suggests an increase in the activity of ribosomes. So far , success in nuclear morphometric analysis to look for the nuclear roundness factor (NRF) had been demonstrated with success in predicting radiation response in Wilms' tumor and prostate cancer (Gearhart et al 1995 and Hurwitz et al 1999). In this study, we examined AgNOR score, nuclear, and nucleolar morphometry before and during radiotherapy as a predictor of radiosensitivity.

Materials and Methods

Patient selection

Twenty-six documented cases of squamous cell cancers involving head and neck region were recruited for this study. The initial clinical assessment especially the initial clinical

tumor volume of the palpable disease were recorded in the analysis (Annexure-1). The clinical tumor volume were measured as the maximum size on three dimensions. These and recorded before, during (on the 5th day) and 6 weeks after above radiotherapy schedule (Fig-1).

Radiotherapy schedule

Radiotherapy was delivered by a 6 MV linear accelerator, using two or three field technique. The dose fractionation was 30 Gy in 10 fractions over 2 weeks period. In case of parallel opposed portal the dose was calculated at the mid-plane, but in the lower neck field dose was calculated at the d-max. Individualized BDS cast were made for daily reproducibility in upper neck region tumors.

Cytological evaluation

Fine needle aspiration cytology (FNAC) was performed to obtain tissue materials. The tissue fluids were obtained from the measurable nodes which were in the radiotherapy portal. The FNAC was performed before radiotherapy, on the 5th day while on treatment and on the 6th weeks after completion of the course in case of persistent disease. The cytology slides were smeared on conventional glass slides with frosted ends and then immersed in 95% alcohol as fixative. The slides were stained with silver nitrate smear and processed. The nuclear organizer regions (NOR) were counted from the high power microscope (400x magnification)as numbers of dots (nucleolus) per a given number of nucleus counted (Fig-2). The same cytology slides were subjected to nuclear morphometric analysis using an image analyzer (Leica Qwin, Germany) at the same magnification. The greatest diameter of the nucleus and nucleolus were determined by

this method. We used 400x magnification for the determination of nuclear or nucleolar size (Fig-3 and 4) for all the cases.

Statistical analysis

The values of the AgNOR score and nuclear morphometric parameters were recorded for each patient and for the each sample. The outcome were analyzed for the response to radiotherapy and further disease course. The *Wilcoxon Signed Ranked test* was applied to look for difference in the tumor regression according to the nuclear morphometry and AgNOR score.

Results

There were 26 patients who completed the above treatment schedule consisting of 6 females and 20 males. The median age of the patient population was 44 years. AgNOR score data were available in 12 patients (Table-1), nuclear morphometry and nucleaolar morphometry was determined in 9 patients (Table-2). The failure to determine the nuclear morphometric and AgNOR score in all cases was related to sampling error, failure to obtain cellular material, and regression of tumour after radiotherapy. The primary tumor were distributed in nasopharynx (11), larynx & hypopharynx (5) , metastatic neck nodes (4) and miscellaneous tumors (6) of the head and neck.

Radiotherapy

All 26 patients received schedule fractionation radiotherapy scheme. Following a tumor dose of 30 Gy in 10 fractions over 2 weeks, the patients were assessed for the tumor

response on day 5, day 10 and day 28. They were categorized as complete response (CR), partial response (PR) and/or no response (NR). Fourteen patients (54%) achieved complete response, 6 patients partial response (23%) and remaining 6 no response (23%) to radiotherapy. The conversion rate after scheduled radiotherapy from palliative intent to radical was observed in 18 (68%) patients after 6 weeks of radiotherapy. Patients achieving complete response showed superior survival than partial response to radiotherapy (Fig-5).

Cytology evaluation

Accurate sampling was possible in 54 aspiration attempts. After few fractions of radiotherapy, patients showed good response to radiation making it difficult to obtain good tissue samples. Twenty patients (76%) underwent initial cytology (cytology-1) which yielded good cellular material, 10 patients (38%) yielded good cellular aspirate after 5th day of radiotherapy (cytology-2) and only 3 patients (12%) had successful 3 rd cytology.

Nuclear morphometry

The greatest diameter of the nucleus and nucleolus were measured [Fig-3 and 4 μm]. The average diameter of the nucleolus and nucleus was 2.92 μm (range 1.09-11.66 μm) and nucleus was 11.073 μm (range 7.70-16.6μm) [Table-2] respectively. Patients whose initial cytology showed large nuclei had more treatment failures and clinical progression of disease than those patients whose cancer cells showed small nuclei. When the nuclear diameter increase after a given course of radiotherapy, there was improved local control and mentainance of response [p 0.008] (Table-3 and Fig-6). Another

interesting observation was that the tumor volume was indirectly proportional to the nuclear volume with a p value of 0.003 (Fig-7).

AgNOR score

Manual AgNOR dot count was done for 35 slides by counting number of AgNOR dots per given number of nucleus counted. Paired AgNOR count before and after radiotherapy was possible in only 12 patients. The mean AgNOR score was 3 dots per nucleus (range 1.2 to 7 dots per nucleus). Patients with high AgNOR score showed higher disease progression and metastasis than those with low AgNOR score (Table-1). The patients who showed a decrease trend in the number of AgNOR dots per nucleus after initial radiotherapy showed an improvement in local control than those with increase in the number of AgNOR score.

Follow up

The patients were advised for regular follow up at an interval of every two months. The median follow up interval was 7 months with a range of 4 to 20 months.

Discussion

This is a prospective study to evaluate the value of AgNOR score, nuclear diameter and nucleolar diameter before and during a course of fractionated radiotherapy to predict radiation response. From this study, albeit a small sample size, we observed that, nuclear size of the tumor cells are indirectly proportional to the clinical tumor volume. Similarly clinical tumor volume is indirectly proportional to the local control by radiotherapy. The number of AgNOR dots was directly proportional to the radiation failures. The final outcome was analyzed at a median follow up duration of 7 months (4-20 months).

Silver nitrate staining for the nuclear organizer region (AgNOR) counts per nucleus is being used in many cancers to predict response to radiation and/or outcome of treatment. In a study on 10 patients, Kossard et al studied AgNOR dots per nucleus in small cell melanoma. He found a variation of AgNOR count of 5.83 in small cell melanoma, 8.49 in superficial spreading melanoma, and 2.71 among dermal nevi (Kossard et al 1995). Thus it suggests that higher AgNOR score predicts an aggressive tumor. In our study too, those cancers with a high AgNOR score per nucleus showed an aggressive disease course. Similar study done by Yue et al in 1999, also showed hyperactivity of malignant cells in those with high AgNOR score in head and neck cancers (Yue et al 1999). In a study from Japan evaluation of AgNOR score in oral cavity cancers shown that, a rise in the AgNOR dots signify a responding tumor to preoperative course of radiotherapy (Kinoshita et al 1996). Their findings were in contrary to ours, which suggest that an increase in the number of AgNOR dots per nucleus following radiotherapy denotes a relentless disease course.

The nucleus and nucleolus are the main constituent of a cell whether it is malignant or benign. Under light microscope, nucleolus look like a dot-like structure situated in the center of the nucleus or slightly displaced towards inner side of the nuclear membrane. Nucleolus are basically in reticular array or as compact structures. It has a fibrillar center, a vacuolar portion and a nucleolus associated chromatin. Thus nucleolus is consisted of dense fibrils and granules which appear as dark staining area of varying intensity

(Nixdorf-Bergweiler et al 1997). Nucleolus is responsible for ribosome production and transcription of r-RNA. Nucleolus is very sensitive to change of ribosomal DNA synthesis. Cytochemical studies have shown a marked increase in the amount of AgNOR scores with large nucleoli implying a large level of ribosomal production. In our study the mean diameter of nucleolus was 2.92μm (range 1.09-11.66 μm).

The treatment with radiation therapy is based on the principles of tumor factors like site, size, and histological grade of the tumor. Patients with stage III and IV head and neck cancers are treated with a fixed dose of radiation. But increasing body of evidences shows that, the response to radiation is not constant even if we keep the tumor-related parameters constant. This wide variation of the radioresponsiveness to fractionated radiotherapy is probably indicated by an inherent cytological factor influencing the behavior of the cancer after radiation exposure. Fibroblasts from patients suffering from ataxia telangiectasia are 2 to 3 times more sensitive than the normal cells (Begg 1999). Thus the response to radiation is a product of wide range of cellular parameters like, nuclear, nucleolar, chromosomal, apoptosis and genetic factors.

The cancers are commonly classified according to histology and graded according to the degree of their differentiation as well differentiated, moderately differentiated and poorly differentiated cancers. The poorly differentiated cancers seems to be more sensitive to radiation than well differentiated tumors. These histology-based variation are demonstrated in cervical cancers and some head and neck cancers. Sometimes

histopathology do not correlate with clinical curability (Meyer and Wang 1971). In our study we concluded that there is no correlation between histopathology grade and response to radiotherapy.

Colony assay of the tumor cells have been implicated for predicting radiation response based on the fraction of cells surviving a particular fraction of radiation dose, defined as the ability to undergo at least 6 doublings. Intrinsic radiosensitivity measurement with SF2 analysis have been demonstrated by Fertil and Malaise, who analyzed the published studies of in vitro radiosensitivity of tumor cell lines from different histologic types and found a general correlation with clinical curability (Fertil and Malaise 1985).

West and his colleagues studied the SF2 assay of radiotherapy treated squamous cell cancers of the cervix. Tumour SF2 values in vitro from fresh biopsy material using colony formation in agar were found to correlate highly with outcome. Patients with SF2 value more than median value had significantly worse survival rate than SF2 value below median (West et al 1993).

An ideal radiation sensitivity tests should be specific, sensitive, cost effective and can be practiced routinely. Chromosomal damage assay and radiosensitive gene assay are a few new tools for the prediction of radiosensitivity (Brown 1992). The first study on radiosensitivity test was demonstrated on the serial cytology tests from cancer cervix called Grahms grading (Grahm et al 1947). Subsequently the studies have been

duplicated by Gupta and colleagues (Gupta et al 1987). Following a course of radiation, there is alteration of the cellular and nuclear morphology. There may be an increase in size of the nucleus, whereby the nuclear material become more condensed with appearance of more nuclei. Bhattathiri et al studied serial cytologic features for the analysis of micronuclei formation during fractionated radiotherapy and found a correlation between micronuclei formation and treatment outcome (Bhattathiti et al 1998).

Nuclear morphometric analysis is a quantity predictive process which has been successfully employed in predicting present treatment outcome in a number of malignancies. Nuclear and nucleolar size estimation is a new concept for the assessment of tumor radiosensitivity. The initial estimation on nuclear and nucleolar morphometry was demonstrated by Mc Lean and colleagues. They found a correlation between large nucleoli and patient treatment outcome. From the study on induction of micronucleation, nuclear budding and multinucleation produced by fractionated radiotherapy, Bhattathiri et al showed that multinucleation had the greatest relation with radiation sensitivity. This study suggested that the injury to the cytokinetic apparatus was important in determining tumor radiosensitivity (Bhattathiri et al 1998). Another study by Memon et al also demonstrated nuclear changes as a predictor of radioresponsiveness in oral cancer patients on radiotherapy (Memon and Jafaray 1970).

In our study, we measured the diameter of nucleus of the tumor cells before and during a fractionated course of radiotherapy. Those patients who showed an increase in the

diameter of nucleus size following radiotherapy achieved good local control of disease than those who showed otherwise The above finding was statistically significant (p value 0.008). Following an initial course of radiotherapy, the nucleus of the cell increases and gradually lead to fragmentation, leading to reproductive death of the cell.

Another dimension of radioresponsiveness is nuclear roundness factor (NRF). In a study on prostate cancers by Horwith et al those who underwent radical radiotherapy, they noticed positive correlation of NRF to radiosensitiveness (Hurwitz et al 1999). The authors used automated imaging devise to determine NRF. Sampling from aspiration cytology is an optimal method to evaluate nuclear morphometric analysis (Liu et al 1996), however studies using conventional hematoxyline-eosin histopathological slides to determine nuclear morphometry had been done (Hamilton and Allen 1995). In our experience, the failure to obtain samples during radiotherapy was high and it is more marked on subsequent aspiration cytology while the tumor is regressing, most probably due to technical shortcomings.

In conclusion, the response of cancers to radiation is basically governed by inherent radiosensitivity to the tumor cells, proportion of hypoxic cells component and repopulation of the resistant clones of cells. The first component of radiosensitivity can be predicted by the use of nuclear morphometry before starting radiotherapy or during a course of radiotherapy. In borderline clinical situations where the decision to either use radiotherapy or surgery is in dilemma, this test might help to decide the treatment arm

before completion of radiotherapy. However a study on a large number of patients need to be done before it could be recommended routinely.

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Table- 1. AgNOR score and response to radiation

Response	AgNOR score
Good response	
Case-1	2.46/nucleus
Case-2	2.17/nucleus
Case-3	2.7/nucleus
Case-4	2.36/nucleus
Case-5	1.36/nucleus
Case-6	1.4/nucleus
Case-7	1.7/nucleus
Poor response	
Case-1	4.46/nucleus
Case-2	2.6/nucleus
Case-3	7/nucleus
Case-4	3/nucleus
Case-5	2.6/nucleus

6/7 patients with < 2.5 dots/nucleus had good response and 5/5 patients with > 2.5 dots/nucleus had poor response.

Table-2. Nuclear and nucleolar diameters in studied patients

Sl.Number	Nuclear diameter in µm		Nucleolar diameter in µm	
	Before RT	During RT	Before RT	During RT
1.	8.77(2.3)	16.62(3.7)	5.59(3.07)	11.66(1.06)
2.	14.91(4.8)	16.2(1.9)	4.13(1.09)	4.69(1.06)
3.	16.21(1.02)	7.70(1.002)	3.78(0.8)	1.77(0.34)
4.	8.32(1.6)	11.56(2.5)	2.91(0.6)	2.65(0.8)
5.	10.26(2.9)	16.11(3.1)	1.09(0.2)	3.45(1.36)
6.	9.98(2.98)	9.75(2.37)	2.64(1.09)	2.4(0.7)
7.	10.51(3.19)	8.88(2.19)	3.38(1.23)	2.89(1.09)
8.	9.53(1.3)	8.48(2.796)	1.43(1.05)	1.41(0.32)
9.	10.917(2.93)	9.51(0.77)	2.62(0.69)	4.16(0.69)

Mean nuclear diameter 11.073 µm and nucleolar diameter 2.92 µm.

Table-3: Nuclear diameters before and during radiotherapy (Standard deviation inside parenthesis) with survival.

Nuclear Diameter in μm Pre RT (SD in ±)	Nuclear Diameter in μm Post RT (SD in ±)	Outcome on last visit
1.8.77 (2.305)	16.62 (3.729)	14 M NED
2.14.9131 (4.8438)	16.2046 (1.9221)	15M NED
3. 16.2046 (1.0221)	7.70 (1.002)	6M PD
4.10.917 (2.934)	9.51 (0.772)	17 PD
8.32 (1.677)	11.565 (2.54)	12 NED
8.91 (3.198)	16.116 (3.008)	12 NED
9.988 (2.985)	9.755 (2.371)	6 PD
10.51 (3.193)	8.88 (2.196)	7 PD
9.532 (1.304)	8.488 (2.796)	7 PD

Abbreviations: NED no evidence of disease, PD progressive disease, M months

Fig-1.

STUDY DESIGN

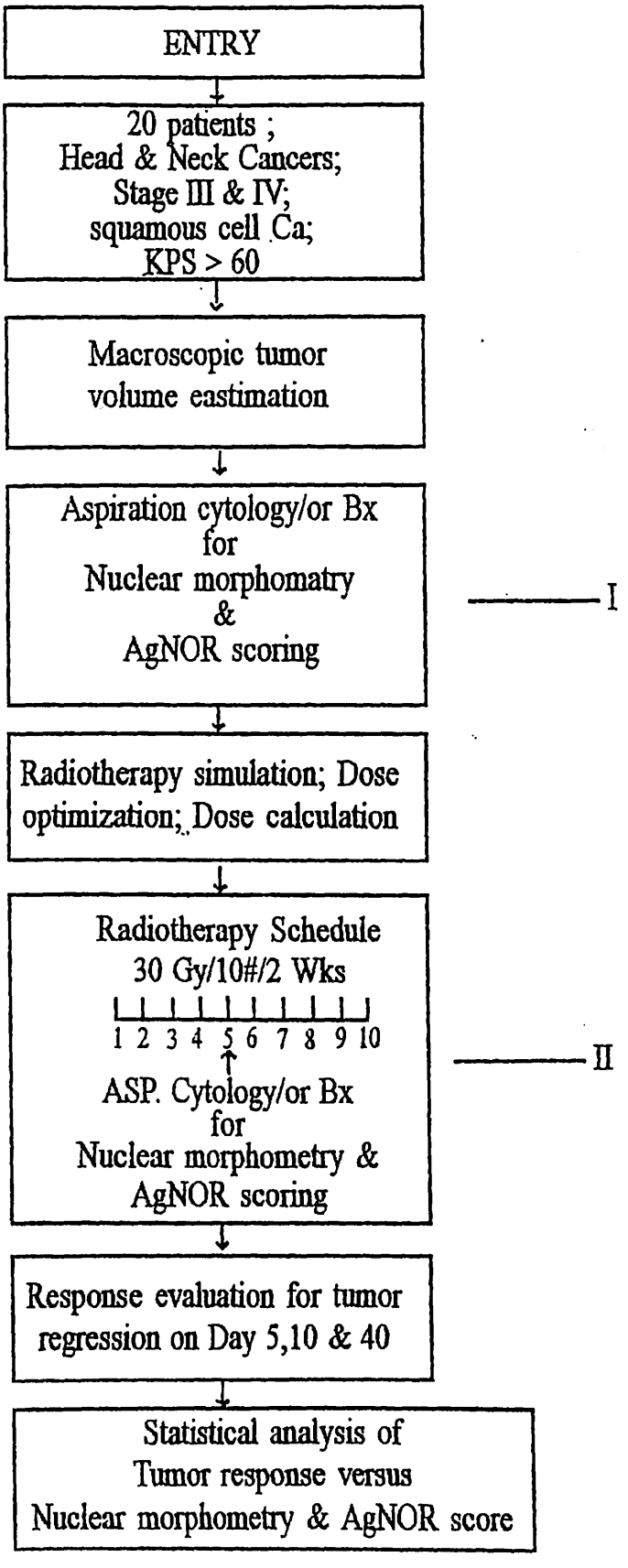


Fig-2. Photomicrograph showing studded nucleolar dots
Counted per nucleus to determine AgNOR score
Magnification 400x

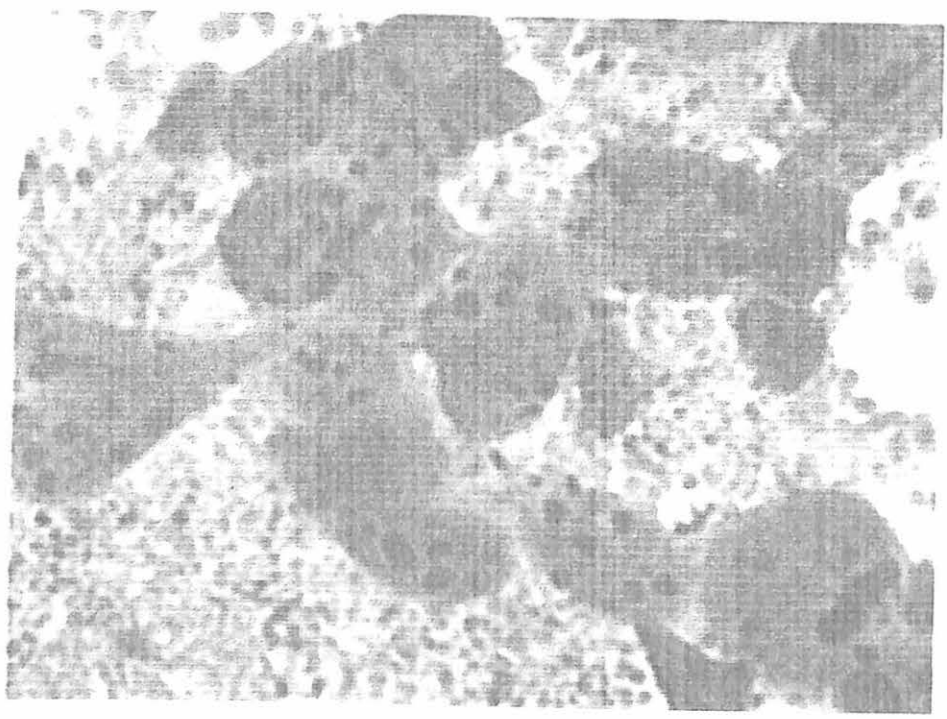


Fig-3. Photomicrograph showing numerous nucleoli laden nucleus before giving radiotherapy
Magnification 400x

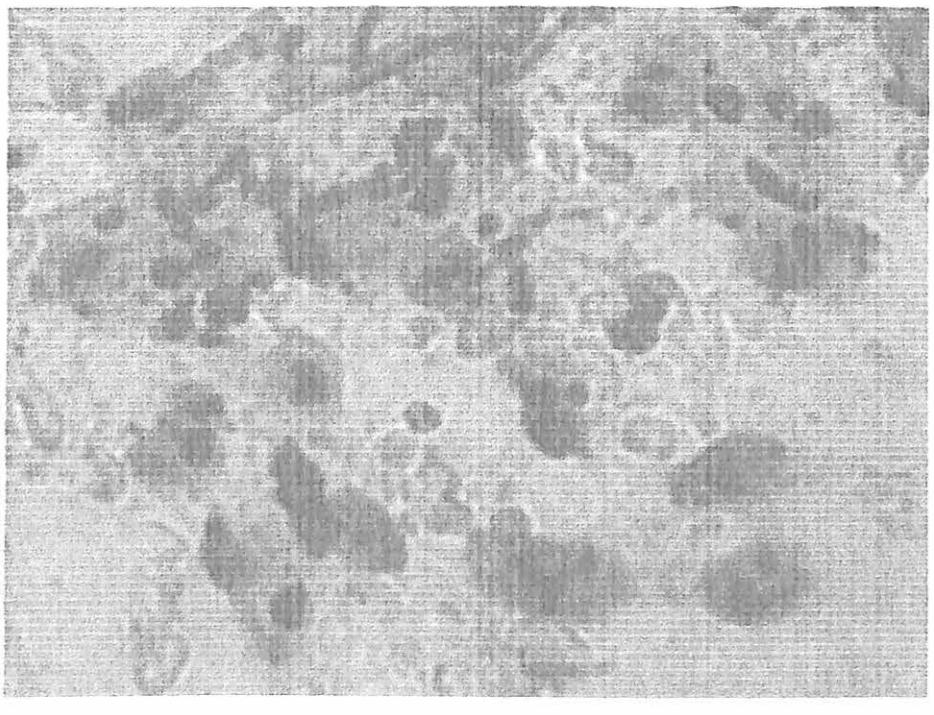


Fig-4. Photomicrograph showing clumped and bizzare nucleoli containing nucleus during radiotherapy
Magnification 400x

Fig-5.

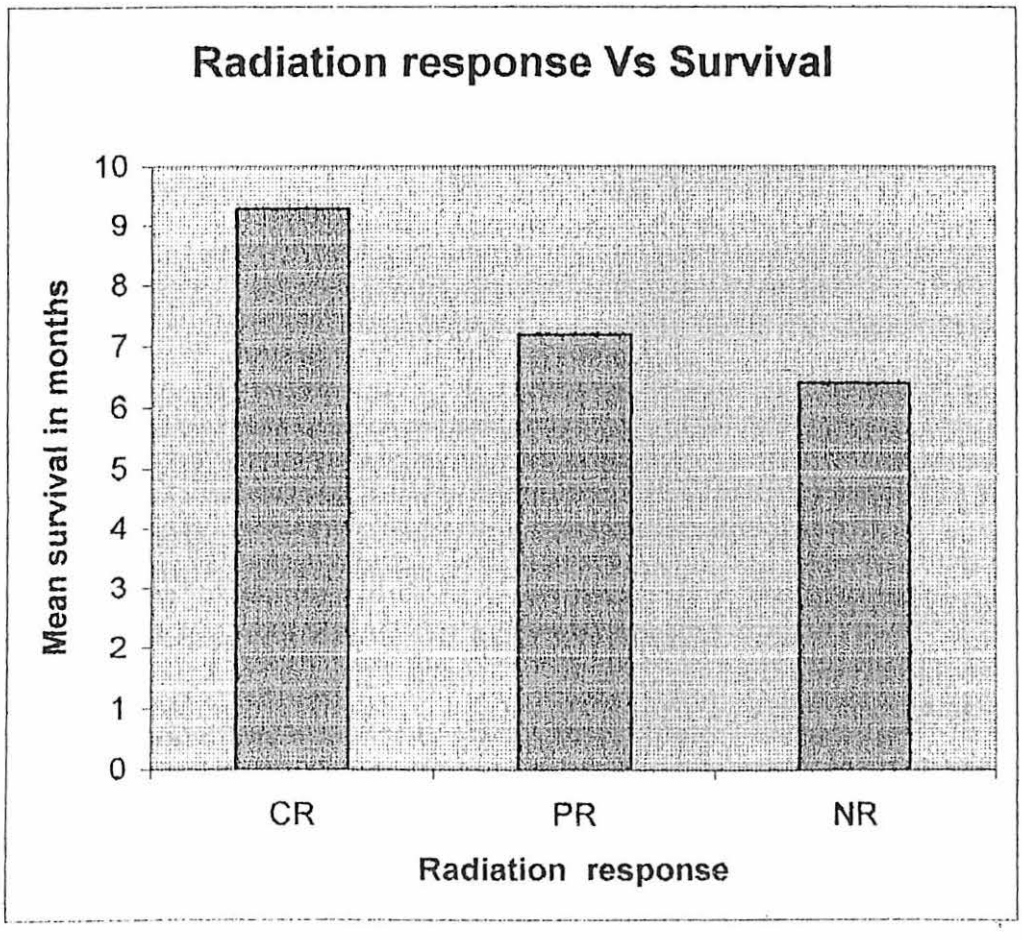

Radiation response Vs Survival
Mean survival in months
10
9
8
7
6
5
4
3
2
1
0
CR
PR
NR
Radiation response

Fig-6.

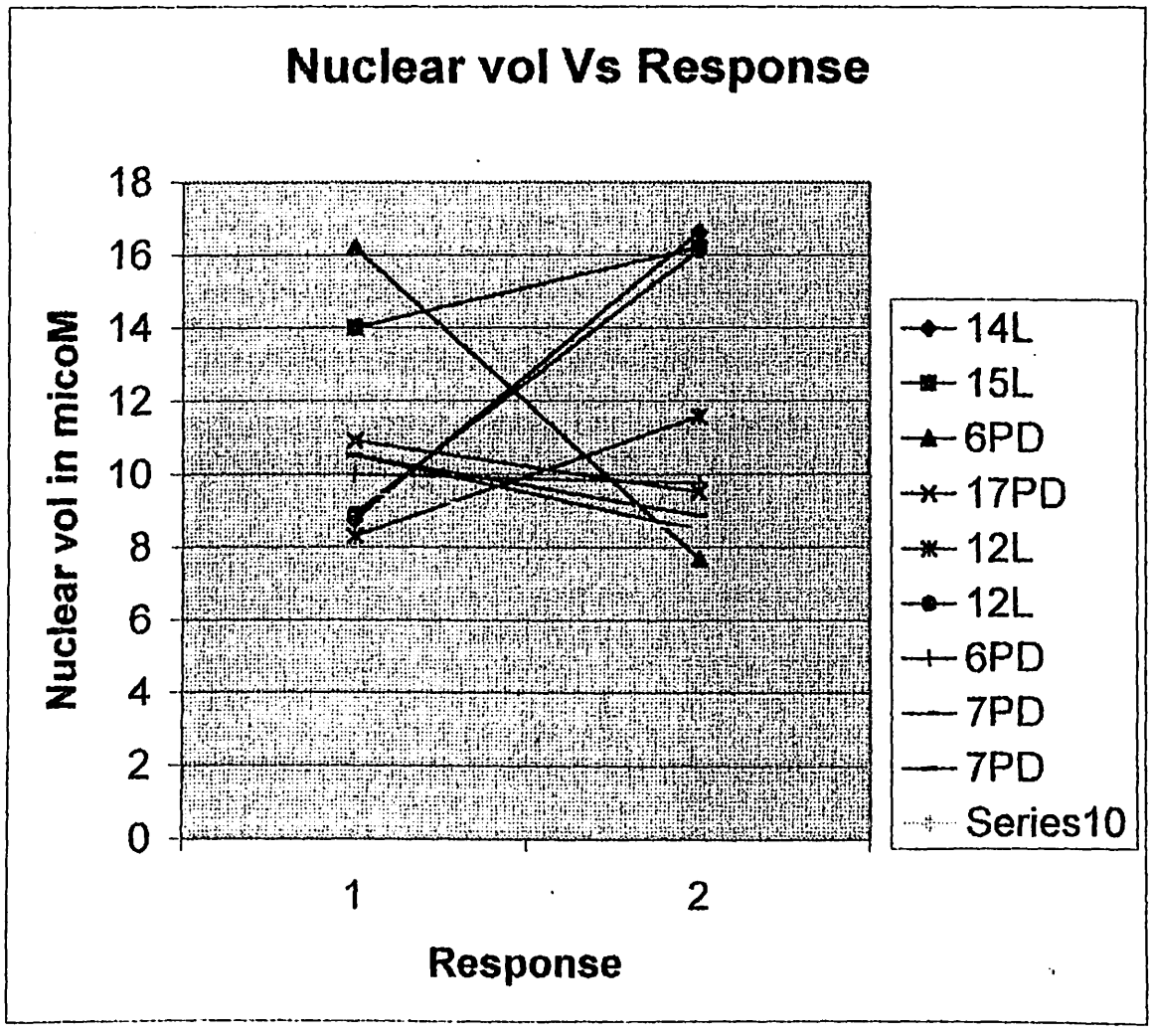
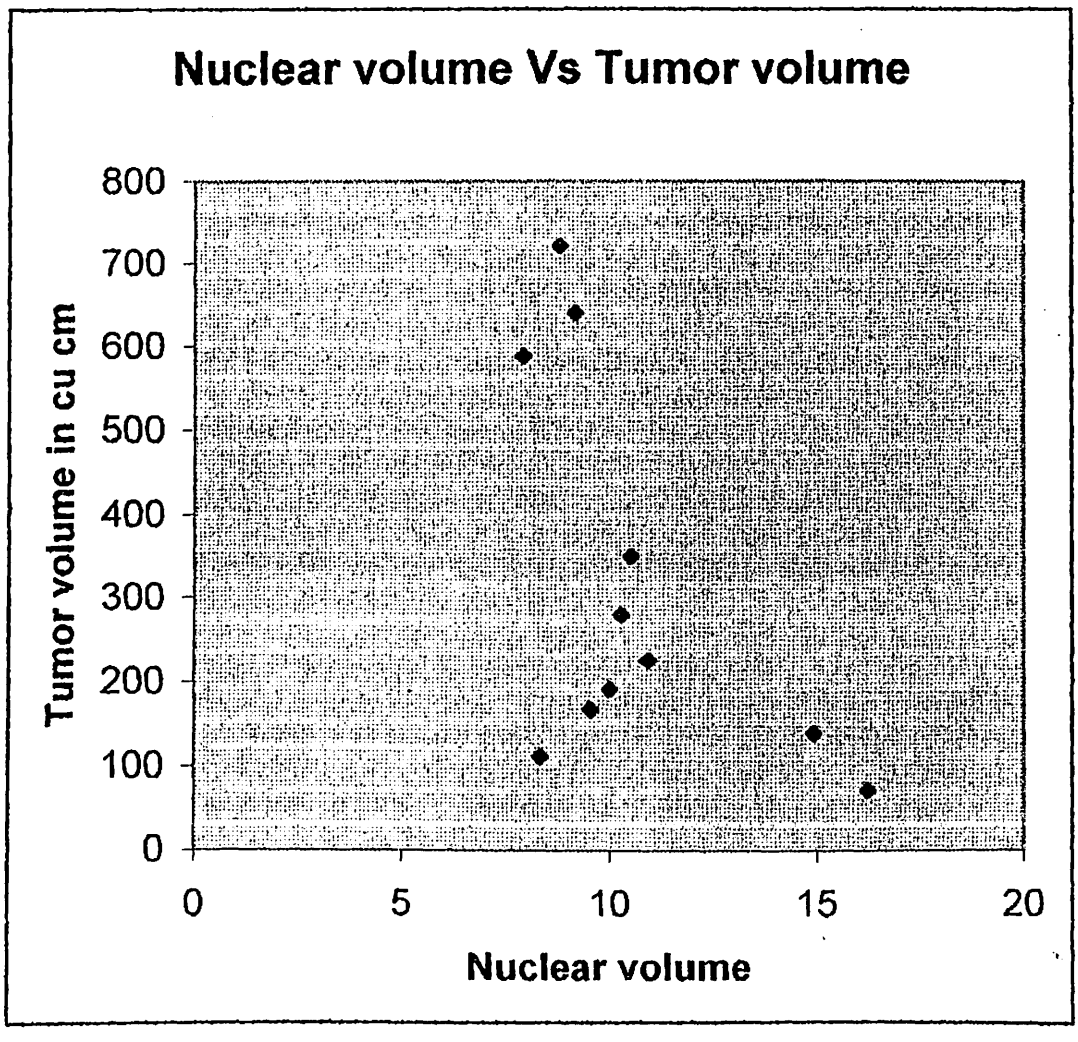

Nuclear vol Vs Response
Nuclear vol in micoM
18
16
14
12
10
8
6
4
2
0
1
2
Response
14L
15L
6PD
17PD
12L
12L
6PD
7PD
7PD
Series10

Fig-7.


Nuclear volume Vs Tumor volume
Tumor volume in cu cm
800
700
600
500
400
300
200
100
0
0
5
10
15
20
Nuclear volume

FOR
NUCLEAR MORPHOMETRY
AND
Ag NOR SCORING

Annexure-1.

PROFORMA FOR RESEACH PROTOCOL

(NUCLEAR MORPHOMETRY & AgNOR SCORE IN HEAD & NECK CANCER RADIOTHERAPY)

Patient No : _____

Name : _____ K.P. No: _____

HUSM Regd.No : _____

Age: _____ Sex _____, Nationality _____, Race _____

Diagnosis : _____

Stage (TNM) _____ ECDG. (P.S) _____

Smoking (alcohol intake history) if any _____

Local examination [Description with figure] :

Histopathology : P-Number _____

X-ray Neck
PNS
Base skull