



# Journal of Applied Sciences

ISSN 1812-5654

**science**  
alert

**ANSI***net*  
an open access publisher  
<http://ansinet.com>

RESEARCH ARTICLE

OPEN ACCESS

DOI: 10.3923/jas.2015.582.587

## Sentinel Lymph Node Detection Using Methylene Blue in Iranian Patients with Early Stage Cervical Cancer

<sup>1</sup>Soheila Aminimoghaddam, <sup>1</sup>Leila Shadman, <sup>4</sup>Raziyeh Sadat Hashemi, <sup>2,3</sup>Zahra Mohammadi and <sup>5</sup>Fatemeh Mahmoudzadeh

<sup>1</sup>Department of Obstetrics and Gynecology, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran

<sup>2</sup>Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

<sup>3</sup>Osteoporosis Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

<sup>4</sup>Department of Obstetrics and Gynecology, Faculty of Medicine, Baghiatallah University of Medical Sciences, Tehran, Iran

<sup>5</sup>Mazandaran University of Medical Sciences, Sari Medical Student, Tehran, Iran

### ARTICLE INFO

#### Article History:

Received: May 31, 2014

Accepted: November 15, 2014

#### Corresponding Author:

Zahra Mohammadi,  
Endocrinology and Metabolism  
Research Center,  
Endocrinology and Metabolism Clinical  
Sciences Institute,  
Tehran University of Medical Sciences,  
Tehran, Iran  
Tel: (+21)88220072

### ABSTRACT

Cervical cancer is one of the most common diseases in women and is associated with high mortality. The aim this study is to evaluate the feasibility of Sentinel Lymph Node (SLN) detection in patients with cervical cancer using the methylene blue dye. Patients in the early stages of cervical cancer were enrolled in this study. Methylene blue, 4 mL, was injected into the cervical peritumoral area in 24 cases. Surgically removed lymph nodes were examined by pathology for the blue lymph nodes that were considered as SLNs. Sensitivity and specificity of this test are, respectively 89 and 83%. Detection rate based on the different nodes with the highest rate of 37.5% was observed in obturator. Various studies have shown that concurrent use of methyl blue method has the highest rate of SLN identification.

**Key words:** Cervical cancer, SLN, sentinel lymph node, methyl blue

### INTRODUCTION

Cervical cancer is one of the most common neoplastic that according to the World report, half-million new people are infected by this disease annually. Prevalence of Cervical cancer is significantly high after breast cancer (Franco *et al.*, 2003; Anderson and Simonton, 2001). It affects about 16 per 100,000 women per year and kills about 9 per 100,000 per year (IARC., 2002). In this disease both genetic and environmental factors, such as smoking, parity, hormone therapy, nutrition and infection are effective. Although, *Human papillomavirus* (HPV) infection appears to be a necessary factor in the development of almost all cases of cervical cancer (Madeleine *et al.*, 2001; Merrill *et al.*, 2005; Moreno *et al.*, 2002). Based on studies, cervical cancer is the

sixth most common cancer in women in united state. So, it has a high prevalence in developed countries (Krivak *et al.*, 2007). In 1998, about 12,800 women were diagnosed in the US and about 4,800 died (Canavan and Doshi, 2000). In the Iranian population, the prevalence of cervical cancer is about 0.18-1.02 (Jafari *et al.*, 2008; Talebi and Poor, 1999).

General and local extensions are two important ways for the cervical cancer to metastasize, although distant metastasis is most frequently in advanced stages. So, local treatment, such as surgery and radiotherapy, has been the main management of cervical cancer. Overall, the incidence of pelvic lymphatic metastasis in patients with stages I and II are in the range of 16-0 and 31-25%, respectively (Malur *et al.*, 2001).

Generally lymphadenectomy for patients without metastatic lymph nodes are not necessary due to complications from surgery. Sentinel Lymph Node (SLN) is the first node to be involved in lymphatic spread. The pathologic status of this specific node presumably reflects the overall status of the whole regional drainage area. Surgical decisions and treatment based on SLN for reproductive cancers, breast and melanoma has been associated with great success (Morton *et al.*, 1999; Giuliano *et al.*, 1994; Veronesi *et al.*, 1997; Ung, 2004; Sandelin, 2004; Ikeda *et al.*, 2004; Leong, 2004; Levenback *et al.*, 1995, 2001; Moore *et al.*, 2003a, b).

Since 2000, the use of this method for cervical cancer was studied. Methyl blue was used initially (Medl *et al.*, 2000; Dargent *et al.*, 2000; O'Boyle *et al.*, 2000; Dargent and Enria, 2003) then radiocolloid (Kamprath *et al.*, 2000; Lantzschi *et al.*, 2001; Martinez-Palones *et al.*, 2004; Angiolia *et al.*, 2005). The studies indicated that hybrid model has been verified and effective (Malur *et al.*, 2001; Verheijen *et al.*, 2000; Levenback *et al.*, 2002; Plante *et al.*, 2003; Buist *et al.*, 2003; Lambaudie *et al.*, 2003; Barranger *et al.*, 2004; Niikura *et al.*, 2004; Gil-Moreno *et al.*, 2005). In these methods, patients should be in the early stages of cancer (Levenback *et al.*, 2002; Plante *et al.*, 2003; Buist *et al.*, 2003; Lambaudie *et al.*, 2003; Barranger *et al.*, 2004; Niikura *et al.*, 2004; Gil-Moreno *et al.*, 2005).

In developing countries, due to the high incidence of cervical cancer has been attempted on such a low cost method to be used for diagnosis. So methyl blue instead of radiocolloid has been investigated in several studies. Use of radiocolloid is time consuming and costly (O'Boyle *et al.*, 2000; Martinez-Palones *et al.*, 2004; Wang *et al.*, 2004).

The response rate of methyl blue is not high but many studies indicated that if there is proper injection rate can be associated with an appropriate response (Dargent *et al.*, 2000). Various colored powder has been used in different countries. So according to studies we can say, respectively patent blue, isosulfan blue, methylene blue used in Europe, USA, China (Franco *et al.*, 2003; Veronesi *et al.*, 1997; Ung, 2004; Medl *et al.*, 2000; Dargent *et al.*, 2000; O'Boyle *et al.*, 2000; Kamprath *et al.*, 2000; Martinez-Palones *et al.*, 2004). So the aim of this study is SLN examination by methyl blue.

## MATERIALS AND METHODS

In this cross-sectional study, from 2012-2014, 25 patients with early stage (I-IIA) cervical cancer diagnosed in the oncology units of Firoozgar and Baghiatallah hospitals (Iran) were enrolled. All patients undergoing radiotherapy were excluded so one patient was excluded of study. And, we excluded patients treated with neoadjuvant and enlarged lymph nodes. The study was performed after approval by the Scientific and Ethical Committee of Iran University of Medical Sciences and explained to the patients before surgery. Informed consent was obtained from every patient enrolled in

this study. Before surgery, under direct observation, 4 mL methylene blue was injected into the cervix peritumorally (mainly at 3, 6, 9 and 12 o'clock position) in cases. In each of these parts 0.5 cc superficial and 0.5 cc deep was injected. Interval between the injection and the incision was between 20-35 min. Pelvic lymphadenectomy was carried out. All blue nodes were considered sentinel nodes through intraoperative direct inspection. The number and location of SLNs were documented. All removed nodes were sent for pathology testing. So, the pathologic diagnosis was as the gold standard in this study. All removed nodes were examined through routine hematoxylin and eosin (H and E) staining. And also for more information, immunohistochemistry was another test that using in this examination.

SLNs step-sectioned at the interval of 1 mm and the non-sentinel lymph nodes (non-SLNs) removed from 41 patients, were examined through routine hematoxylin and eosin (H and E) staining. For SLNs diagnosed as tumor-free by routine H and E staining, one additional slide of each SLN was immunostained using an anticytokeratin antibody (ZM-0069, Zymed, USA). In the other 40 patients, only routine H and E staining (one or two sections per node) was done for all removed nodes.

**Statistical analysis:** Statistical analysis was performed using SPSS software (version 18.0). The p-value<0.05 was considered statistically significant. The following equations were used:

$$\text{Detection rate} = \frac{\text{Patients with successful SLN identification}}{\text{Patients enrolled}}$$

$$\text{Positive Predictive Value (PPV)} = \frac{\text{No. of patients (methyl blue and pathology)}}{\text{No. of patients with positive test (methyl blue)}}$$

$$\text{Negative Predictive Value (NPV)} = \frac{\text{No. of healthy subjects (methyl blue and pathology)}}{\text{No. of subjects with a negative test (methyl blue)}}$$

Limitations of this study are the lack of access to patients with inclusion and exclusion criteria, time-consuming and costly process.

## RESULTS

Clinical characteristics of the studies population are presented in Table 1. The median and range of patients age was 10.24±48.50 and 29-65 years old, respectively. Average tumor size is 1.06±3.46. And tumor size was varied from 1-5 cm. Also the average time between injection and surgery was 27.8±4.67 min.

Reproductive characteristics of the study population are shown in Table 1.

The parity was divided in two groups (≤4 and >4). About 54.2% women had children more than 4.

As you can see in Fig. 1, 37.5, 33.3 and 29.2% of people are located in IB1, IB2 and IIA1, respectively.

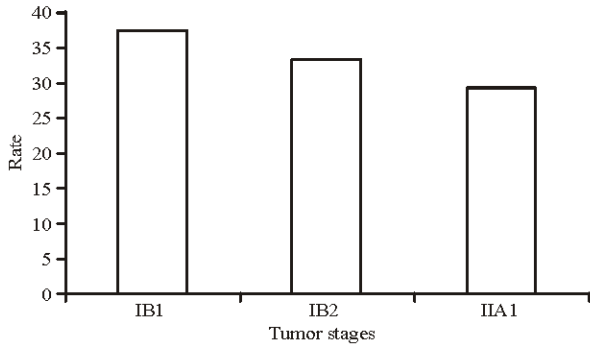


Fig. 1: Rates in different staging of tumor categories (%)

Characteristic groups	No.	Percentage
<b>Age</b>		
28-35	3	12.5
36-45	5	20.8
46-55	10	41.7
>56	6	25.0
<b>Tumor size</b>		
≤4 cm	8	33.3
>4 cm	16	66.7
<b>Staging of tumor</b>		
IB1	9	37.5
IB2	8	33.3
IIA1	7	29.2
<b>Reproductive characteristics</b>		
	Range	Mean
Gravity	7-2	4.33±1.66
Parity	7-2	3.96±1.73
abortion	2-0	0.40±0.64
Live child	6-2	3.90±1.60

Table 2: Rate of positive staining with methyl blue and pathologic response in different nodes

Parameters	Number of positive responses methyl blue		Number of positive responses Pathology	
	N	%	N	%
Right external iliac	6	25.0	2	8.30
Left external iliac	8	33.3	6	25.00
Right obturator	5	20.8	2	8.30
Left obturator	10	41.7	9	37.50
Right inguinal	0	0.0	0	0.00
Left inguinal	1	4.2	0	0.00

In total, people are categorized in 3 levels based on the colorization of SLN, one level without color, second level with single color and third level to more than one color.

There is no significant difference in the overall SLN detection efficiency and tumor size. Though there is no significant relation between overall detection rates and time injection until surgery too.

According to Table 2 and Fig. 2 the differences between rates of positive staining with methyl blue and pathologic response in different nodes is evident.

The results indicated that PPV in right external iliac, left external iliac, right obturator and left obturator lymph nodes was 33, 50, 40 and 90%, respectively. Overall, PPV of methyl

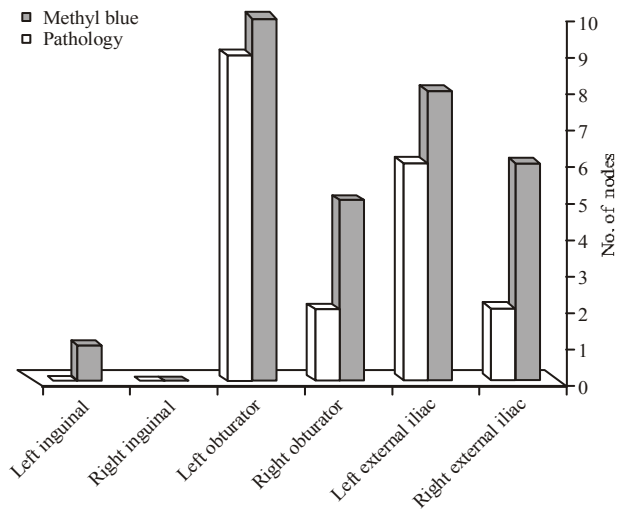


Fig. 2: Compare the number of nodes involved in methyl blue and pathological test

Table 3: Detection rate of methyl blue test on different nodes (SLN)

Lymph nodes	Detection rate		
	Patients with successful SLN identification	Patients enrolled	Percentage
Right external iliac	24	2	8.33
Left external iliac	24	4	16.66
Right obturator	24	2	8.33
Left obturator	24	9	37.50

blue testing in the evaluation of the SLN was 58%. And also, NPV in right external iliac, right obturator and left obturator lymph nodes was 100% and about left external iliac reported 87%. Totally negative predictive value is 97%. Sensitivity and specificity of this test are respectively 89 and 83%. Detection rate based on the different nodes with the highest rate of 37.5% was observed in obturator (Table 3).

## DISCUSSION

Based on the results of studies the detection rate of SLN by blue dye has reported 83.3% (Di Stefano *et al.*, 2005). In the present study, 24 patients were evaluated by methyl blue and the results indicated that the detection rate is the highest rate in obturator lymph node.

In various studies, doses of methyl blue has been considered as a variable and the results have shown that low doses of this substance can reduce the level of detection (Di Stefano *et al.*, 2005; Sheng *et al.*, 2004). It was experimentally observed that the full 4 cc injection of methyl blue, increased detection rate.

In several studies blue dye was injected into the cervix peritumorally, mainly at 2, 4, 8 and 10 o'clock position. In present investigation injection is done at 3, 6, 9 and 12 o'clock position. The results show that the injection in this position is

practical and comfortable. And also in these hour position, probability of injection in lymph nodes increased. In this study, the mean time injection of methyl blue to surgery is  $27.8 \pm 4.67$ . And there is no significant relation between detection rate and this time. It is noteworthy, that the study was conducted have reported similar results (Di Stefano *et al.*, 2005).

The highest detection rate observed in obturator lymph node that, the studies by Sheng *et al.* (2004) and Yuan *et al.* (2007) have reported similar results. Although, individual studies showed different results (Angiolia *et al.*, 2005; Niikura *et al.*, 2004; Gil-Moreno *et al.*, 2005; Rob *et al.*, 2005; Rhim *et al.*, 2002).

In the present study, the sensitivity of this test was 89%. A study was conducted in New York by Beatrice Cormier the sensitivity of methyl blue was 87.5%. Generally, in several studies, the sensitivity of methyl blue varies from 77-100% (Cormier *et al.*, 2011; Roy *et al.*, 2011). Also, in evaluating the specificity of methyl blue, 83% was reported.

Various studies have shown that concurrent use of methyl blue and radioisotope methods has the highest rate of SLN identification (Roy *et al.*, 2011). In the present study, due to the limitations just methyl blue has been investigated. Therefore, a further study with a mixed procedure is recommended.

In the present study, Enlarged and macroscopic lymph nodes were excluded. Because these kinds of nodes may be blocked by tumor cells, thus preventing the migration of the injected dye or because of blockage of the lymph node capsule by tumor cell emboli again is preventing the dye from entering the node (Plante *et al.*, 2003).

SLN identification on each side of the pelvis represents its involvement but there is exception in parametrial lymph node. These nodes are very close to the cervix so there is problem to identify nodes (Plante *et al.*, 2003). This point increases the false positive nodes. So in the present study, parametrial lymph nodes have not been evaluated.

Based on the present study is the first national assessment, the positive predictive value is 58%. It seems that one of the limitations of this study is the sample size, so further studies with larger sample size are recommended.

Finally, we can by SLN Mapping as the gold standard, diagnosis and treat patients with early cervical cancer. The present data demonstrate that methylene blue is the high quality and cost less test.

On the other side, removing out the looking healthy tissue (baft) also is an invasive action which will be decreased.

#### ACKNOWLEDGMENT

We thank Iran University of Medical Sciences and all the patients in cooperation are appreciated.

#### REFERENCES

Anderson, G. and O.C. Simonton, 2001. Cancer: 50 Essential Things to Do. Saunders, USA.

- Angiolia, R., I. Palaiaa, C. Cipriani, L. Muzii, M. Calcagno, G. Gullotta and P.B. Panici, 2005. Role of sentinel lymph node biopsy procedure in cervical cancer: A critical point of view. *Gynecol. Oncol.*, 96: 504-509.
- Barranger, E., A. Cortez, S. Uzan, P. Callard and E. Darai, 2004. Value of intraoperative imprint cytology of sentinel nodes in patients with cervical cancer. *Gynecol. Oncol.*, 94: 175-180.
- Buist, M.R., R.J. Pijpers, A. van Lingen, P.J. van Diest, J. Dijkstra, P. Kenemans and R.H.M. Verheijen, 2003. Laparoscopic detection of sentinel lymph nodes followed by lymph node dissection in patients with early stage cervical cancer. *Gynecol. Oncol.*, 90: 290-296.
- Canavan, T.P. and N.R. Doshi, 2000. Cervical cancer. *Am. Family Physician*, 61: 1369-1376.
- Cormier, B., J.P. Diaz, K. Shih, R.M. Sampson and Y. Sonoda *et al.*, 2011. Establishing a sentinel lymph node mapping algorithm for the treatment of early cervical cancer. *Gynecol. Oncol.*, 122: 275-280.
- Dargent, D. and R. Enria, 2003. Laparoscopic assessment of the sentinel lymph nodes in early cervical cancer. Technique-preliminary results and future developments. *Crit. Rev. Oncol. Hematol.*, 48: 305-310.
- Dargent, D., X. Martin and P. Mathevet, 2000. Laparoscopic assessment of the sentinel lymph node in early stage cervical cancer. *Gynecol. Oncol.*, 79: 411-415.
- Di Stefano, A.B., G. Asquaviva, G. Garozzo, M. Barbic and B. Cvjeticanin *et al.*, 2005. Lymph node mapping and sentinel node detection in patients with cervical carcinoma: A 2-year experience. *Gynecol. Oncol.*, 99: 671-679.
- Franco, E.L., N.F. Schlecht and D. Saslow, 2003. The epidemiology of cervical cancer. *Cancer J.*, 99: 348-359.
- Gil-Moreno, A., B. Diaz-Feijoo, I. Roca, O. Puig and M.A. Perez-Benavente *et al.*, 2005. Total laparoscopic radical hysterectomy with intraoperative sentinel node identification in patients with early invasive cervical cancer. *Gynecol. Oncol.*, 96: 187-193.
- Giuliano A.E., D.M. Kirgan, J.M. Geunther and D.L. Morton, 1994. Lymphatic mapping and sentinel lymphadenectomy for breast cancer. *Ann. Surg.*, 220: 391-401.
- IARC., 2002. GLOBOCAN 2002 database: Summary table by cancer. [http://web.archive.org/web/20080616085344/http://www-dep.iarc.fr/GLOBOCAN/Table1\\_sell.htm](http://web.archive.org/web/20080616085344/http://www-dep.iarc.fr/GLOBOCAN/Table1_sell.htm).
- Ikeda, T., H. Jinno, H. Fujii and M. Kitajima, 2004. Recent development of sentinel lymph node biopsy for breast cancer in Japan. *Asian J. Surg.*, 27: 275-278.
- Jafari, S.M., M. Halimi, A.D. Tabrizi and J. Shahamfar, 2008. Prevalence of for precancerous and invasive cancer lesions of Cervix Tabriz 2003-2005. *Iran. J. Obstetr. Gynecol. Infertil.*, 10: 63-78.
- Kamprath, S., M. Possover and A. Schnaider, 2000. Laparoscopic sentinel node detection in patients with cervical cancer. *Am. J. Obstet. Gynecol.*, Vol. 182. 10.1067/mob.2000.104144

- Krivak, T.H.C., J.W. Macbroom and J.C. Elkas, 2007. Cervical and Vaginal Cancer. In: Novak's Gynecology, Berek, J.S. (Eds.). 14th Edn., Williams and Wilkins, Philadelphia, pp: 1403-1456.
- Lambaudie, E., P. Collinet, F. Narducci, Y. Sonoda and T. Papageorgiou *et al.*, 2003. Laparoscopic identification of sentinel lymph nodes in early stage cervical cancer: Prospective study using a combination of patent blue dye injection and technetium radiocolloid injection. *Gynecol. Oncol.*, 89: 84-87.
- Lantzsch, T., M. Wolters, J. Grimm, T. Mende, J. Buchmann, G. Sliutz and H. Koelbl, 2001. Sentinel node procedure in Ib cervical cancer: A preliminary series. *Br. J. Cancer*, 85: 791-794.
- Leong, S.P.L., 2004. Selective sentinel lymphadenectomy for breast cancer in the United States. *Asian J. Surg.*, 27: 268-274.
- Levenback, C., T.W. Burke, M. Morris, A. Malpica, K.R. Lucas and D.M. Gershenson, 1995. Potential applications of intraoperative lymphatic mapping in vulvar cancer. *Gynecol. Oncol.*, 59: 216-220.
- Levenback, C., R.L. Coleman, T.W. Burke, D. Bodurka-Bevers, J.K. Wolf and D.M. Gershenson, 2001. Intraoperative lymphatic mapping and sentinel node identification with blue dye in patients with vulvar cancer. *Gynecol. Oncol.*, 83: 276-281.
- Levenback, C., R.L. Coleman, T.W. Burke, W.M. Lin, W. Erdman, M. Deavers and E.S. Delpassand, 2002. Lymphatic mapping and sentinel node identification in patients with cervix cancer undergoing radical hysterectomy and pelvic lymphadenectomy. *J. Clin. Oncol.*, 20: 688-693.
- Madeleine, M.M., J.R. Daling, S.M. Schwartz, K. Shera and B. McKnight *et al.*, 2001. Human papillomavirus and long term oral contraceptive Use increase the risk of adenocarcinoma *in situ* of the cervix. *Cancer Epidemiol. Biomarkers Prev.*, 10: 171-177.
- Malur, S., N. Krause, C. Kohler and A. Schneider, 2001. Sentinel lymph node detection in patients with cervical cancer. *Gynecol. Oncol.*, 80: 254-257.
- Martinez-Palones, J.M., A. Gil-Moreno, M.A. Perez-Benavente, I. Roca and J. Xercavins, 2004. Intraoperative sentinel node identification in early stage cervical cancer using a combination of radiolabeled albumin injection and isosulfan blue dye injection. *Gynecol. Oncol.*, 92: 845-850.
- Medl, M., C. Peters-Engl, P. Schutz, M. Vesely and P. Sevelde, 2000. First report of lymphatic mapping with isosulfan blue dye and sentinel node biopsy in cervical cancer. *Anticancer Res.*, 20: 1133-1134.
- Merill, R.M., S. Fugal, L.B. Novilla and MC. Raphael, 2005. Cancer risk associated with early and late maternal age at first birth. *Gynecol. Oncol.*, 96: 583-593.
- Moore, R.G., C.O. Granai, W. Gajewski, M. Gordinier and M.M. Steinhoff, 2003a. Parthologic evaluation of inguinal sentinel lymph nodes in vulvar cancer patients: A comparison of immunohistochemical staining versus ultrastaging with hematoxylin and eosin staining. *Gynecol. Oncol.*, 91: 378-382.
- Moore, R.G., S.E. DePasquale, M.M. Steinhoff, W. Gajewski, M. Steller, R. Noto and S. Falkenberry, 2003b. Sentinel node identification and ability to detect metastatic tumor to inguinal lymph nodes in squamous cell cancer of the vulva. *Gynecol. Oncol.*, 89: 475-479.
- Moreno, V., F.X. Bosch, N. Munoz, C.J. Meijer and K.V. Shah *et al.*, 2002. Effect of oral contraceptives on risk of cervical cancer in woman with human papillomavirus infection: The IARC multicentric case-control study. *Lancet*, 359: 1085-1092.
- Morton, D.L., J.F. Thompson, R. Essner, R. Elashoff and S.L. Stern *et al.*, 1999. Validation of accuracy of intraoperative lymphatic mapping and sentinel lymphadenectomy for early-stage melanoma: A multicenter trial. *Ann. Surg.*, 4: 453-463.
- Niikura, H., C. Okamura, J. Akahira, T. Takano, K. Ito, K. Okamura, K. Okamura and N. Yaegashi, 2004. Sentinel lymph node detection in early cervical cancer with combination <sup>99m</sup>Tc phytate and patent blue. *Gynecol. Oncol.*, 94: 528-532.
- O'Boyle, J.D., R.L. Coleman, S.G. Bernstein, S. Lifshitz, C.Y. Muller and D.S. Miller, 2000. Intraoperative lymphatic mapping in cervix cancer patients undergoing radical hysterectomy: A pilot study. *Gynecol. Oncol.*, 79: 238-243.
- Plante, M., M.C. Renaud, B. Tetu, F. Harel and M. Roy, 2003. Laparoscopic sentinel node mapping in early-stage cervical cancer. *Gynecol. Oncol.*, 91: 494-503.
- Rhim, C.C., J.S. Park, S.N. Bae and S.E. Namkoong, 2002. Sentinel node biopsy as an indicator for pelvic nodes dissection in early stage cervical cancer. *J. Korean Med. Sci.*, 17: 507-511.
- Rob, L., P. Strnad, H. Robova, M. Charvat, M. Pluta, D. Schlegerova and M. Hrehorcak, 2005. Study of lymphatic mapping and sentinel node identification in early stage cervical cancer. *Gynecol. Oncol.*, 98: 281-288.
- Roy, M., G. Bouchard-Fortier, I. Popa, J. Gregoire, M.C. Renaud, B. Tetu and M. Plante, 2011. Value of sentinel node mapping in cancer of the cervix. *Gynecol. Oncol.*, 122: 269-274.
- Sandelinm, K., 2004. Current European studies of sentinel lymph node biopsy for breast cancer. *Asian J. Surg.*, 27: 291-293.
- Sheng, X.G., D.P. Li, N.F. Liu, Q.S. Li, L. Tang, H.Q. Li and C.H. Lu, 2004. [Clinical significance of sentinel lymph nodes detection in patients with early stage cervical cancer]. *Zhonghua Fu-Chanke Zazhi*, 39: 10-14, (In Chinese).

- Talebi, A. and S.A. Poor, 1999. Frequency of pre-malignancy and malignancy in over 46000 Pap smears in Isfahan. *J. Shahid Sadoughi Univ. Med. Sci. Health Services*, 7: 40-44.
- Ung, O.A., 2004. Australasian experience and trials in sentinel lymph node biopsy: The RACS SNAC trial. *Asian J. Surg.*, 27: 284-290.
- Verheijen, R.H., R. Pijpers, P.J. van Diest, C.W. Burger, M.R. Buist and P. Kenemans, 2000. Sentinel node detection in cervical cancer. *Obstet. Gynecol.*, 96: 135-138.
- Veronesi, U., G. Paganelli, V. Galimberti, G. Viale and S. Zurrada *et al.*, 1997. Sentinel-node biopsy to avoid axillary dissection in breast cancer with clinically negative lymph-nodes. *Lancet*, 349: 1864-1867.
- Wang, H.Y., J.M. Sun and J. Tang, 2004. [Sentinel lymph nodes detection in patients with cervical cancer undergoing radical hysterectomy]. *Zhonghua Fu-Chanke Zazhi*, 39: 7-9.
- Yuan, S.H., Y. Xiong, M. Wei, X.J. Yan, H.Z. Zhang, Y.X. Zeng and L.Z. Liang, 2007. Sentinel lymph node detection using methylene blue in patients with early stage cervical cancer. *Gynecol. Oncol.*, 106: 147-152.