

Synergo®

Last Updated Friday, 14 November 2008

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Innovations in treating Bladder Cancer and Synergo Workshop In collaboration with Rome Catholic University, Prof. PF Bassi, December 2, 2005

Rome, Italy: WebCafe's review of the presentations

{/niftybox}Medical Enterprises: Synergo®

Intravesical Hyperthermia for non-muscle-invasive bladder cancer - improves effectiveness of Mitomycin C

For a list of institutions in Europe using this method, see below

Update Dec. 2005- References - Partial List of Published articles, see below

Local microwave-induced hyperthermia has a therapeutical potential for the treatment of many solid tumors. In bladder cancer it has shown itself to be especially useful when combined with intravesical chemotherapy for non-muscle-invasive tumors.. After extensive laboratory investigations, recent advances in miniaturized technology have led to the development of equipment which is specially designed for delivering thermo-chemotherapy (also known as thermal intravesical chemotherapy) to the human bladder.

Ongoing human and animal studies conducted in Europe and Israel dating back some 12 years or more have proven that microwave-induced hyperthermia combined with intravesical mitomycin C is a feasible, effective and safe conservative approach for those with [high risk] multiple and recurrent non-muscle-invasive bladder tumors when other treatment strategies have failed, and/or when cystectomy is contra-indicated or the patient refuses to undergo radical surgery.

Recent clinical experience has shown that treatments with Synergo® are highly efficient and give a lower recurrence rate than traditional methods. Synergo® technology has been approved by the European Standard Authorities (CE) and is now in the process of receiving FDA approval in the US.

In one randomized study, the patients having the new treatment showed a much lower recurrence rate (20%) than patients receiving conventional treatment (70%).

During the last decade this system was mainly used as an alternative to TURB. When clinically used for this indication, this system was shown to be effective, and safe. In a randomized trial it was more effective than intravesical chemotherapy alone.¹

With the system now in clinical practice, a 915 MHz microwave applicator is inserted into the bladder via a special catheter. In addition, a set of thermocouples are inserted to control the temperature of the bladder wall layers which are heated to a temperature of 42 +/- 2 degree Celcius (approximately 104 degrees Fahrenheit +/- 1 degree). The drug is then pumped out and re-instilled, as a way of avoid overheating. Everything is monitored by a computerized unit with special software.

Each treatment lasts one hour, no major systemic side effects are observed, with local side effects being tolerable and temporary; no regional or general anesthetic is required, and patients can resume normal daily activities the same day.

All studies performed to date have shown the benefit of the Synergo® system over TUR or TUR+intravesical chemo with improved clinical results, lower recurrence rates and a reduced need for cystectomy. (see list below)

Synergo® treatments are performed in Germany, Israel and Italy, Holland, Switzerland, Austria, France and Belgium. For more info see article: New Technology For Superficial Bladder Cancer; <http://www.medinews.com/GMEDTS32olcgi/ts.cgi?tsurl=0.55.1236.0.0> and manufacturer's website, Medical Enterprises

www.Medical-Enterprises.com Medical Enterprises Europe B.V.

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References - Partial List of Published articles-

To read all abstracts about thermo-chemotherapy at the National Library of Medicine click [here](#)

Thermo-Chemotherapy for intermediate or high-risk recurrent superficial bladder cancer patients. *Ann Oncol.*2005 Apr;16(40):585-9. Moskovitz B, Meyer G, Kravtsov A, Gross M, Kastin A, Biton K, Nativ O.

Effect of Hyperthermia on the Cytotoxicity of Four Chemotherapeutic Agents Currently Used for the Treatment of Transitional Cell Carcinoma of the Bladder - An in Vitro Study. Van der Heijden A.G, Verhaegh G, Cornelius F. J. J, Schalken J.A, Witjes J.A. *J Urol* Vol. 173, 1375-1380, 2005.

The Effect of Hyperthermia on Mitomycin-C Induced Cytotoxicity in Four Human Bladder Cancer Cell Lines. Van der Heijden A.G, Cornelius F. J. J, Verhaegh G, O'Donnell M.A, Schalken J.A, Witjes J.A. *Eur Urol.* 2004 Nov;46(5):670-674.

Preliminary European Results of Local Microwave Hyperthermia and Chemotherapy Treatment in Intermediate or High Risk Superficial Transitional Cell Carcinoma of the Bladder. Van der Heijden A.G, Kiemeny L.A, Gofrit O.N, Nativ O, Sidi A, Leib Z, Colombo R, Naspro R, Pavone M, Baniel J, Hasner F, Witjes J.A. *Eur Urol* 46:65-72;2004.

Combined Local Bladder Hyperthermia and Intravesical Chemotherapy for the Treatment of High Grade Superficial Bladder Cancer. Gofrit O.N, Shapiro A, Pode D, Sidi A, Nativ O, Leib Z, Witjes J.A, Van Der Heijden A.G, Naspro R, Colombo R. *Urol* 63(3):466-471;2004.

Multicentric Study Comparing Intravesical Chemotherapy Alone and With Local Microwave Hyperthermia for Prophylaxis of Recurrence of Superficial Transitional Cell Carcinoma. Colombo R, Da Pozzo L.F, Salonia A, Rigatti P, Leib Z, Baniel J, Caldarera E, Pavone-Macaluso M. *J Clin Oncol*. 21:4270-4276;2003.

Neoadjuvant combined microwave induced local hyperthermia and topical chemotherapy versus chemotherapy alone for superficial bladder cancer.

J Urol 155:1227-1232;1996. Colombo R, Da Pozzo L.F, Lev A, Freschi M, Gallus G, Rigatti P.

Synergo for chemo-resection:

Thermo-chemotherapy and electromotive drug administration of mitomycin C in superficial bladder cancer eradication. *Eur Urol* 39:95-100;2001. Colombo R, Brausi M, Da Pozzo L.F, Salonia A, Montorsi F, Scattoni V, Roscigno M, Rigatti P

Medline Abstract, excerpt:

"A higher complete response rate on marker lesion was observed after thermo-chemotherapy compared to other administration methods. **CONCLUSION:** The intravesical administration of mitomycin C can be safely performed in the form of both thermo-chemotherapy and electromotive drug approach with an increased ablative success rate on small superficial tumor involving only minimal local side effects." .

Intravesical electromotive mitomycin C versus passive transport mitomycin C for high risk superficial bladder cancer: a prospective randomized study.

Di Stasi SM, Giannantoni A, Stephen RL, Capelli G, Navarra P, Massoud R, Vespasiani G. Departments of Urology and Clinical Biochemistry, Tor Vergata University, Via Torrice n. 4, 00189 Rome, Italy; *J Urol*. 2003 Sep;170(3):777-82. PMID: 12913696

CONCLUSIONS: Intravesical electromotive administration increases bladder uptake of MMC, resulting in an improved response rate in cases of high risk superficial bladder cancer. Medline abstract

Local microwave hyperthermia and intravesical chemotherapy as bladder sparing treatment for select multifocal and unresectable superficial bladder tumors. Colombo R; Da Pozzo LF; Lev A; Salonia A; Rigatti P; Leib Z; Servadio C; Caldarera E; Pavone-Macaluso M

Department of Urology, Scientific Institute H. San Raffaele, Milan, Italy.

J Urol 1998 Mar;159(3):783-7 PMID: 9474148 UI: 98134423 **CONCLUSIONS:** Microwave induced hyperthermia combined with intravesical mitomycin C seems to be a feasible, safe and elective approach for conservative treatment of multifocal and recurrent superficial bladder tumors when other treatment strategies have failed. Medline Abstract

.Study of the synergy of microwave hyperthermia/intravesical chemotherapy in the prevention of recurrences of superficial tumors of the bladder Mauroy B; Bonnal JI; Prevost B; Chive M; Lhotellier V; Sozanski JP; Vanseymortier L; Stefaniak X Service Univeritaire d'Urologie, CHU de Lille-Roubaix, France Prog Urol 1999 Feb; 9(1):69-80 PMID: 10212955 UI:99229425 CONCLUSION: A possible clinical application is potentiation of the action of mitomycin C by hyperthermia in the prevention of recurrent superficial bladder tumours, achieving increased efficacy and/or a decreased number of instillations. Medline Abstract

Multicentric Study Comparing Intravesical Chemotherapy Alone and With

Local Microwave Hyperthermia for Prophylaxis of Recurrence of Superficial

Transitional Cell Carcinoma. J Clin Oncol. 21:4270-4276;2003. Colombo R, Da Pozzo L.F, Salonia A, Rigatti P, Leib Z, Baniel J, Caldarera E, Pavone-Macaluso M. Medline Abstract, excerpt:

"Survival analysis of the 75 assessable patients demonstrated a highly significant difference in the survival curves in favor of thermochemotherapy. ..In our series, endovesical thermochemotherapy appears to be more effective than standard endovesical chemotherapy as an adjuvant treatment for superficial bladder tumors at 24-month follow-up, despite an increased but acceptable local toxicity.

Combined intravesical hyperthermia and mitomycin chemotherapy: a preliminary in vivo study.Rath-Wolfson L, Moskovitz B, Dekel Y, Kugel V, Koren R. Department of Pathology, Hasharon Hospital, Rabin Medical Centre, Petah-Tikva, Israel Int J Exp Pathol. 2003 Jun;84(3):145-52. PMID: 12974944

Conclusions: [in animal studies] the control group showed similar changes, some less pronounced. The combined treatment of hyperthermia with mitomycin C did not cause major damage to the urinary bladder or adjacent organs. All changes were superficial and reversible, and the control group showed similar changes, some less pronounced. Although this is an experimental model based on one single session treatment, rather than repeated treatments, it suggests that the approach may be useful in future studies both in models and man. Medine abstract

Effect of local hyperthermia of the bladder on mitomycin C pharmacokinetics during intravesical chemotherapy for the treatment of superficial transitional cell carcinoma. Br J Clin Pharmacol 52:273–278;2001. Paroni R, Salonia A, Lev A, Da Pozzo L.F, Cighetti G, Montorsi F, Rigatti P, Colombo R.

Medline Abstract excerpt:

CONCLUSIONS: Local hyperthermia enhances the systemic absorption of MMC during intravesical chemotherapy for bladder cancer. In the doses used, plasma MMC concentrations were always more than six times lower than those shown to cause toxicity.

Combination of intravesical chemotherapy and hyperthermia for the treatment of superficial bladder cancer: preliminary clinical experience. Crit Rev Oncol Hematol. 47(2):127-39;2003. Colombo R, Salonia A, Da Pozzo L.F, Naspro R, Freschi M, Paroni R, Pavone-Macaluso M, Rigatti P.

Combined Local Bladder Hyperthermia and Intravesical Chemotherapy for the Treatment of High Grade Superficial Bladder Cancer. Accepted for publication in Urology: 2003. Gofrit O.N, Shapiro A, Pode D, Sidi A, Nativ O, Leib Z, Witjes J.A, Van Der Heijden A.G, Naspro R, Colombo R.

Future strategies in the diagnosis, staging and treatment of bladder cancer.

Curr Opin Urol 13(5):389-95;2003. Van der Heijden A.G, Witjes J.A.

Intravesical Chemotherapy: An Update – New Trends and Perspectives.

EAU Update Series 1 (2003) 71-79. Van der Heijden A.G, Witjes J.A.

Locally induced hyperthermia in bladder cancer. Bladder Cancer: Biology, Diagnosis and Management, Chapter 22, Oxford Medical Publication, Ed. K.N. Syrigos & D.G. Skinner, 1999. Rigatti P, Lev A, Da Pozzo L.F, Salonia A, Colombo R.

Local microwave hyperthermia and intravesical chemotherapy as bladder sparing treatment for select multifocal and unresectable superficial bladder tumors. J Urol 159:783-787;1998. Colombo R, Da Pozzo L.F, Lev A, Salonia A, Rigatti P, Leib Z, Servadio C, Caldarera E, Pavone-Macaluso M.

Plasma mitomycin C concentrations determined by HPLC coupled to solid-phase extraction. Clin Chem 43:615-618;1997. Paroni R, Arcelloni C, De Vecchi E, Fermo I, Mauri D, Colombo R.

A new approach using local combined microwave hyperthermia and chemotherapy in superficial transitional bladder carcinoma treatment. J Urol 153:959-963;1995. Colombo R, Lev A, Da Pozzo L.F, Freschi M, Gallus G, Rigatti P.

Combined intravesical chemotherapy with mitomycin C and local bladder microwave-induced hyperthermia as a preoperative therapy for superficial bladder tumors - A preliminary clinical study. Eur Urol 20:204-210;1991. Rigatti R, Lev A, Colombo R.

List of Presentations and Book Chapters - (1991 - 2003)

.
Combined Local Bladder Hyperthermia and Intravesical Chemotherapy for the Treatment of High Grade Superficial Bladder Cancer. Gofrit O.N, Shapiro A, Pode D, Sidi A, Nativ O, Leib Z, Witjes J.A, Van Der Heijden A.G, Naspro R, Colombo R. Presented at the Israel Urology Association Conference, Eilat, 2003.

Neo Adjuvant Treatment Modality in Intermediate- High Risk Superficial Transitional Cell Carcinoma of the Bladder Facing Cystectomy:
A Multicenter Study. Presented at the A.U.A annual congress, Chicago, 2003.
Sidi A, Nativ O, Witjes J.A, Pavone-Macaluso M, Alken P, Shapiro A, Leib, Z, Serretta V, Siegsmund M, Tarnopolsky A, Gofrit O, Van Der Heijden A.G, Da Pozzo L.F, Salonia A, Wald M, Florio A, De Carolis D, Colombo R.

Intravesical Chemotherapy alone versus Intravesical Thermo- Chemotherapy for Prophylaxis of Recurrence of Superficial Transitional Cell Carcinoma: A Multicenter Study. Presented at the A.U.A annual congress, Chicago, 2003. Colombo R, Da Pozzo L.F, Salonia A, Rigatti P, Leib Z, Baniel J, Caldarera E, Pavone-Macaluso M.

Neoadjuvant Combined Microwave Induced Local Hyperthermia and Topical

Chemotherapy in Superficial TCC of Bladder. Presented at the Israeli Urology Association Conference, Eilat, 2002. Tavdy E, Tarnopolsky A, Benjamin S, Mogutin B, Sidi A.

Synergo – chemotherapy treatment in patients with refractory bladder TCC.

Presented at the Israel Urology Association Conference, Eilat, 2001. Gofrit O, Wald M, Sidi A, Nativ O, Pode D, Shapiro A.

Pharmacokinetics of mitomycin C in patients treated with local microwave-

induced hyperthermia. Presented at the XIVth E.A.U. Congress, Stockholm, 1999. Salonia A, Colombo R, Lev A, Da Pozzo L.F, Montorsi F, Rigatti L, Bua L, Rigatti P, Paroni R.

Adjuvant microwave hyperthermia and mitomycin C versus mitomycin C

alone for superficial bladder cancer. Presented at the XIVth E.A.U. Congress, Stockholm, 1999. (Eur Urol 35(2):39;1999). Colombo R, Da Pozzo L.F, Lev A, Gallus G, Salonia A, Freschi M, Rigatti P, Leib Z, Baniel J, Caldarera E, Pavone-Macaluso M.

Thermochemotherapy and electromotive drug administration of mitomycin C

in superficial bladder tumors eradication. A clinical trial on marker lesion.

Presented at the XIVth E.A.U. Congress, Stockholm 1999. (Eur Urol 35(2):25;1999). Colombo R, Brausi M, Da Pozzo L.F, Salonia A, Montorsi F, Scattoni V, Raber M, Rigatti P.

Combined thermo-chemotherapy for recurrent superficial bladder tumors:

Results of a preliminary study using epirubicin. Presented at the XIIIth E.A.U. Congress, Barcelona, 1998. Da Pozzo L.F, Colombo R, Lev A, Salonia A, Rigatti P.

Studio multicentrico randomizzato mitomicina C vs. mitomicina C + ipertermias endocavitaria nella profilassi delle neoplasie vescicali superficiali. Presented at the Società Italiana di Urologia (S.I.U) Congress, 1998. Da Pozzo L.F, Colombo R, Salonia A, Lev A, Grasso M, Montorsi F, Rigatti P, Gallus G, Leib Z, Baniel J, Caldarera E, Biancorosso M, Pavone-Macaluso M.

Microwave hyperthermia + mitomycin C versus mitomycin C alone in the

prophylaxis of superficial transitional bladder cancer. Presented at the A.U.A. Congress, San Diego, CA, 1998. Da Pozzo L.F, Colombo R, Lev A, Gallus G, Salonia A, Rigatti P, Leib Z, Baniel J, Pavone-Macaluso M, Caldarera E.

Quantificazione in HPLC della concentrazione plasmatica di mitomicina C in pazienti affetti da neoplasie vescicali superficiali sottoposti a termochemioterapia topica. Presented at the Società Italiana di Urologia (S.I.U) Congress, 1998. Salonia A, Colombo R, Lev A, Da Pozzo L.F, Rigatti D, Pompa P, Rigatti P, Paroni R, Arcelloni C, De Vecchi E, Fermo I.

Bladder sparing treatment combining local microwave hyperthermia and chemotherapy for multifocal unresectable superficial bladder tumors.

Presented at the A.U.A. Congress, New Orleans, 1997. Da Pozzo L.F, Colombo R, Lev A, Salonia A, Rigatti P, Caldarera E, Pavone-Macaluso M, Leib Z, Servadio C.

Studio multicentrico randomizzato mitomicina C vs. mitomicina C +

ipertermia endocavitaria nella profilassi delle neoplasie vescicali superficiali. Presented at the Società Italiana di Urologia (S.I.U) Congress, 1997. Da Pozzo L.F, Colombo R, Salonia A, Lev A, Grasso M, Montorsi F, Rigatti P, Leib Z, Baniel J, Caldarera E, Pavone-Macaluso M.

Intravesical microwave-induced hyperthermia and mitomycin C for selected

multifocal unresectable superficial bladder tumors. Presented at the XIIthE.A.U Congress, Paris, 1996. Da Pozzo L.F, Colombo R, Lev A, Rigatti P, Leib Z, Servadio C, Caldarera E, Pavone-Macaluso M.

Mitomycin C (MMC) vs. MMC combined with local microwave hyperthermia

(LMWH) as prophylaxis of recurrence of superficial transitional bladder

cancer: A preliminary report. Presented at the XIIthE.A.U Congress, Paris, 1996. Leib Z, Baniel J, Servadio C, Colombo R, Da Pozzo L.F, Lev A, Rigatti P,

Caldarera E, Pavone-Macaluso M.

Patients are being treated with Synergo at the following institutions:

AUSTRIA

Prof. Bartsch, TILAK Clinic Innsbruck

Prof. Bartsch, Clinic Innsbruck

BELGIUM

Prof. Schulman, Dr. Zlotta, Erasme Hospital, Brussels *

Prof. Schulman, Dr. Zlotta, Erasme Hospital, Brussels *

FRANCE

Prof. Martin, Prof. Colombel, Edouard Herriot Hospital, Lyon *

Prof. Gattegno, Tenon Hospital, Paris *

Prof. Hermanowicz, St Joseph Hospital, Marseille

Prof. Houlgatte, Hôpital d'instruction des armées du Val de Grâce, Paris

Prof. Teillac, Saint-Louis Hospital, Paris *

GERMANY

Prof. Alken, Klinikum Mannheim, Mannheim University Hospital

Prof. Chaussy, Krankenhaus Harlaching, Munich *

Prof. Muschter, Diakoniekrankenhaus Urologie, Rotenburg

Prof. Stenzl, Eberhard Karls University, Tuebingen

Prof. Tunn, City Hospital, Offenbach

ISRAEL

Prof. Baniel, Rabin Medical Center, Petah-Tikva

Dr. Leibovitch, Meir Medical Centre, Kefar-Saba

Prof. Kaneti, Soroka Medical Centre, Be'er-Sheva

Prof. Meretik, Rambam Medical Centre, Haifa

Prof. Nativ, Bnai-Zion Hospital, Haifa *

Prof. Pode, Hadassah University Hospital, Jerusalem *

Prof. Sidi, Wolfson Medical Center, Holon *

Prof. Stein, Carmel Medical Center, Haifa

Prof. Nativ, Bnai-Zion Hospital, Haifa *

Prof. Pode, Hadassah University Hospital, Jerusalem *

Prof. Sidi, Wolfson Hospital, Holon *

ITALY

Prof. Barbieri, Urology Dep., Ospedale C.G. Mazzoni, Ascoli Piceno

Prof. Bassi, Urology Dep., Sacro Cuore Catholic University Hospital "A. Gemelli", Rome

Prof. Conti, Urology Dep. Sant'Anna Hospital, Como

Prof. De Cobelli, Urology Dep. European Institute of Oncology, Milan *

Prof. Maffezzini, Urology Dep. Galliera Hospital, Genoa

Prof. Miano, Urology Dep. St. Andrea Hospital, Rome

Prof. Pavone, University Policlinic Hospital, Palermo *

Prof. Pino, Urology Dep, Treviglio Hospital, Treviglio

Prof. Rigatti, Dr.Colombo, HSR Hospital, Milan*

Prof. Vavassori, Urology Dep. Humanitas Gavazzeni, Bergamo

Prof. Barbieri, Ospedale C.G. Mazzoni, Ascoli Piceno

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Prof. De Cobelli, Urology Dep. European Institute of Oncology, Milan *

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Prof. Pino, Azienda Ospedaliera, Ospedale di Treviglio

Prof. Rigatti, Dr.Colombo, HSR Hospital, Milan*

Prof. Rocco, Urology Dep. San Paolo Hospital, Milan

SWITZERLAND

Prof. Studer, Dr. Thalmann, Insehpital, Bern

Prof. Studer, Dr. Thalmann, Insehpital, Bern

THE NETHERLANDS

Dr. Oosterhof, Academic Hospital, Maastricht

Dr. van der Meijden, Jeroen Bosch hospital, Hertogenbosch

Prof. Witjes, University Hospital, Nijmegen *

Dr. van Moorselaar, Universitair Medisch Centrum (UMC), Utrecht

Dr. Oosterhof, Academic Hospital AZM, Maastricht

* Centers participating in the clinical study.

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