The effects of the InterX 5000 on pain reduction in the severe chronic orthopedic patient.

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Introduction

The base technology of the InterX 5000 has clinically been studied extensively in Russia, Europe and with limited use in the United States and Canada. The device, when applied to patients with acute and chronic pain has been shown to effectively reduce pain with serial treatments.[1] [2]

In addition, different site treatments have reduced pains in various areas of the body. The associated observation with serial use has been shown to increase circulation and reduce swelling in the orthopedic patient. The primary mechanism of action is thought to be through afferent C-filament stimulation of nerves breaking a pain arch. However decrease in swelling, increase in circulation, and warmth of the extremity, where the pain is secondary to orthopedic problems implicate possible autonomic nerve effects as seen in reflex sympathetic dystrophies.

The InterX 5000 is a handheld portable electrical neuro stimulator device, which provides electrical stimulation through two conductive electrodes, using skin as a conduit. The signal delivered is a damped, bi-phasic oscillatory waveform.

While the base frequency delivered is 59.3 cycles per second, the number of pulses delivered can be varied from 15 per second to 350 pulses per second. In addition, these pulses can be grouped into bursts of pulses. The power, frequency, pulse duration, pulse grouping and waveform damping can all be controlled by the user.[3]

For any specified user settings, the waveform shape and energy delivered to the body changes as a function of the skin and underlying tissue characteristics. There is an internal load circuit that is designed to create a sharing of the energy output between the device and the body. This interactive nature of the device is a key element to the effectiveness of the device.

The therapist applies the device to the patient's body by holding or moving the electrodes along a variety of locations. There are several techniques which must be learned by the clinician to define the optimum treatment protocol depending upon the patient's complaints and condition. The techniques are based upon an understanding of tissue differences or skin impedance. Changes in tissue impedance can be actively displayed by the InterX 5000 or identified through therapist's observations. Differences are observed as color changes and/or adherence of electrodes to the skin. This "sticky" adherence factor allows a therapist to localize and target the zone of treatment on each patient.

The treatment of severe chronic pain in orthopedic patients varies with the underlying pathologic conditions that cause it. Routinely opiates or derivatives with or without invasive technologies are used to decrease the pain. Opiates are associated with many side effects including; drug dependency, overdosing, insomnia, gastrointestinal side effects, hallucinations, and with overuse, loss of mentation, depression of the central nervous system and often times even death. Invasive technologies such as spinal cord stimulation, sympathectomies, nerve blocks, and pumps, usually

require anesthesia, with its inherent risk, to complete the procedure. If the patient requires surgical implants then the inherent additional surgical risks need also to be addressed. TENS units are currently being used by therapists, but have not been shown to be significantly more effective over placebo when addressing the chronic pain patient. There are no clinically available, "non-invasive" technologies that have been shown to be significantly effective in dealing with the chronic pain patient.

The search for other "non invasive" technologies is underway to reduce risk to patients when dealing with the chronic pain patient. The InterX 5000 has been clinically tested as a biofeedback mechanism and has no known side effects. [4]

Materials and Methods (Study Protocol)

Objective:
The primary objective of the pilot study was to determine if focused short-term treatment (3 days) with the InterX 5000 would reduce pain levels, by three points or greater, on an 11-point numerical rating scale in a group of severe chronic orthopedic patients. Because of the severe chronic nature of the pain, patients actively receiving narcotics were accepted. Of secondary interest was whether or not patients would voluntarily reduce pain medication without increasing pain levels.

Inclusion/Exclusion Criteria:
In order to assess the benefits of the InterX 5000 in reduction of pain, a complex group of orthopedic surgical patients with known chronic severe pain were chosen. In all patients, opiates or their derivatives had been used on a chronic basis. The patients had a multitude of underlying orthopedic problems and the pain was unrelieved with any other treatments of which included sympathetic blocks, local nerve blocks, duragesic patches or use of medications. Concise clinical histories of the patients in the study group are provided in Table 1.

Patients were asked to discontinue any outside treatments for pain relief, including cortisone shots, electrical stimulation, and/or acupuncture. Occupational/physical therapy is considered a compliment to InterX 5000 treatments therefore patients participated in these visits if previously scheduled.

Data Collection:
The patients were provided with a consent to treat, clinical history statement form and a brief pain inventory (see Appendices 1-3). In addition, the therapist completed an intake form which subjectively described pain level and local sites (see Appendix 4). Based on information the therapist evaluated treatment approach and designed protocol to treat local pain site and/or dermatomal nerve regions. The therapist recorded time and treatment protocol which lasted 30-45 minutes. At the end of the treatment the patient was asked questions and a subjective therapist evaluation was performed as recorded by the patient. The before and after treatment evaluations were completed serially for 3 days. At the end of three days the brief pain inventory was filled out by the patient. In addition, physical exams were performed before, during, and after treatment for any additional changes observed in the patient's physical changes in pain medication were also reported. The only additional information obtained in the second and third visit was to record the patients changes in regard to symptamotology since the last visit. (Appendix 5)

Results

Twenty-two patients were classified by identification number to protect privacy. Table 1 reflects an in-depth discussion of the history of the patient participants. The patient was asked to report on a Numeric Rating Scale (NRS) of 1-10 the average pain (AV), pain at the site (PAS) and pain upon activity (Illicit). As was appreciated, the average pain prior to treatment, as seen in Table 2, varied with a range of 2-10, with a median of 6.0 and a mean 6.0. PAS was slightly more intense with a range of 2-10, and median of 6.0 and a mean of 6.1. The Illicit pain ranged from 3-10 with again a median of 7.0 and a mean of 7.0. As can be visualized by this table there was no significant difference in the patient descriptions of their pain.

After the first treatment the AV changed from a range of 0-6 with a median of 2.0 and a mean of 2.3. The PAS ranged from 0 – 6.5 with a median of 2.0 and a mean of 2.3. The Illicit ranged from 0 – 7.5 with a median of 3.5 and a mean of 2.9. These results indicate after the first treatment the AV improved by 62%, the PAS improved by 58% and the illicit pain was improved by 61%. The greatest AV improvements were seen in patient #4, #6, #13, #19, and #20. These patients demonstrated an improvement of greater than 5 points on the 1 – 10 NRS.

Table 3 reflects similar data from Table 2 obtained before and after treatment on Day 2. The median AV score before treatment was 4.5 with a range of 0-10 and a mean of 4.3. The PAS ranged from 0 – 10 with a median of 6.0 and a mean of 4.9. The Illicit ranged from 0 – 10 with a median of 7.0 and a mean of 5.7. The pre-treatment AV on Day 2, as compared to pre-treatment Day 1, improved by 28%, the PAS improved by 19% and the Illicit improved by 18%. This demonstrated a sustained response in the group of patients.

The post treatment AV on Day 2 ranged from 0-5 with a median of 1.0 and a mean of 1.6. The PAS ranged from 0 – 6 with a median of 1.5 and a mean of 2.0. The Illicit ranged from 0 – 6 with a median of 2.0 and a mean of 2.3. The overall improvement after Day 2 as compared to pre-treatment was 73% for the AV, 68% on the PAS and 67% for the Illicit. The greater than 5 point AV improvements were seen in patient #3, #7, #14, #16, and #21.

On Day 3 (Table 4) the pre-treatment AV ranged from 0 – 8 with a median of 2.0 and a mean of 3.1. The PAS ranged from 0 – 9 with a median of 3.3.6 and a mean of 3.8. The Illicit ranged from 0 – 9 with a median of 4.8 and a mean of 4.4. The pre-treatment AV from Day 2 to Day 3 improved an additional 27%, the PAS improved by 27% and the Illicit improved by 23%. This demonstrated a continued improvement after additional treatments.

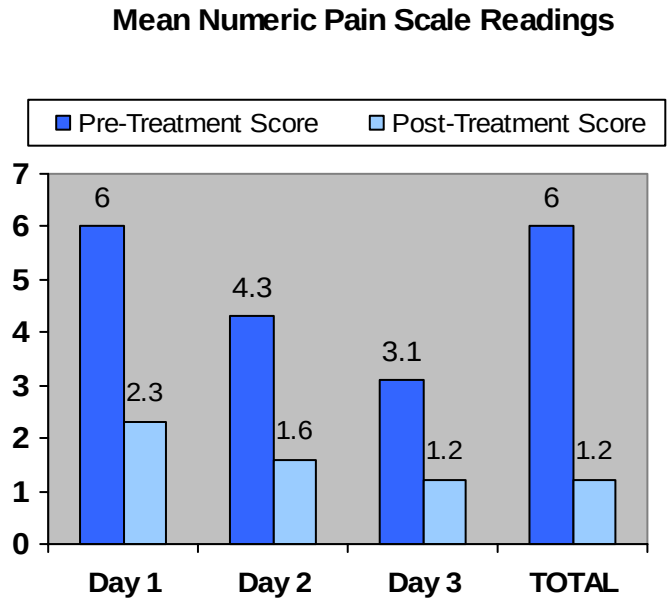
The post treatment AV on Day 3 ranged from 0-6 with a median of 0.0 and a mean of 1.2. The PAS ranged from 0 – 7 with a median of 0.0 and a mean of 1.4. The Illicit ranged from 0 – 7 with a median of 0.3 and a mean of 1.8. The overall improvement after the final treatment on Day 3 as compared to pre-treatment was 79% for the AV, 76% on the PAS and 73% for the Illicit. The greater than 6 point AV improvements over the course of treatment were seen in patient #3, #4, #6, #20, #21, and #22. Although patient #4 experienced a significant reduction in pain immediately post-treatment each day the values were not sustained over a 24-hour period.

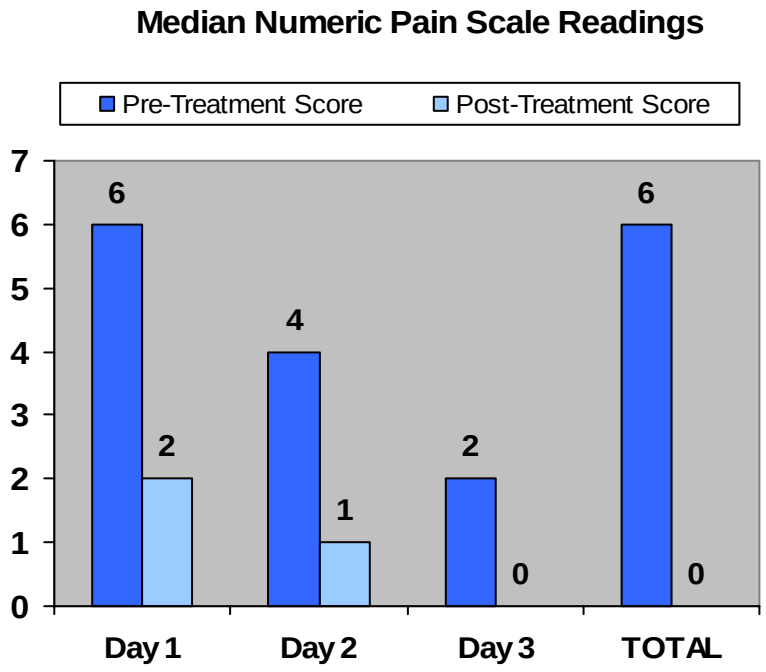
Ten patients began the study on significant pain medication (opiates or derivatives and duragesic patches). Of the group, four patients required duragesic patches. Forty percent (40%) of the patients voluntarily reduced their pain medication requirements (Table 6). Interestingly all of the patients on the duragesic patches voluntarily discontinued the use within the first 24 hours of the study. An additional patient who underwent a shoulder disarticulation, who was semi-lethargic

on numerous pain medications, was lucid and had dramatically decreased his pain medication requirement throughout the treatment period.

Table 5 demonstrates the change in numeric pain score from the beginning of treatment to the end. The AV changed 4.7 points or 79%, the PAS changed 4.6 or 76%, and the Illicit changed 5.1 or 73%.

In addition to the data obtained via forms, two patients demonstrated immediate response to the use of the InterX 5000 with decreased lower extremity swelling, a change in vascular appearance of the skin and increased warmth of the foot. These effects were quite dramatic. Each of these patients had multiple surgeries on the lower extremities with a neuropathic type of pain. An additional patient had an arterial venous malformation of the lower leg; in this patient the skin had a large "port wine" appearance measuring approximately 10x12 cm^2. Interestingly, with treatment this almost visually disappeared. This patient however failed to reduce sustained pain levels.





Discussion

The chronic pain patient is a complex patient with multifactorial inputs and etiologies which may cause the pain. Even with effective treatment strategies, some patients in pain studies will not be expected to improve because of secondary gains, such as monetary, drug dependency or even psycho-social issues. Non-invasive treatment methods to manage chronic severe pain have largely been ineffective for long term treatment, where the etiologic causes persist. The use of pain medicine which has numerous side effects or invasive procedures remains the rule.

This pilot study chose a group of patients which had "known" orthopedic causes for severe pain as reflected in the condensed patient histories in Table 1. These patients had significant complaints of pain in spite of management by invasive procedures and pain medication. The result after Day 3 demonstrated a 79% reduction in AV, 76% in PAS, and a 73% reduction in Illicit. In this complicated group of orthopedic patients, four patients in this group showed no subjective improvement as reflected in their numeric pain scores. One of these patients reported pre-treatment with a pain score of only 2 on the NRS and reported complete pain relief after three treatments. Of significant interest is the mean and median scores post-treatment on Day 3 were 1.2 and 0 for the AV, 1.4 and 0 for the PAS, and 1.8 and 0 for the Illicit groups. This shows the sixteen patients that improved, did so with significant subjective improvement.

The voluntary pain medicine reduction, and the discarded use of the duragesic patches seen in six of the patients is significant (Table 6). This information can be valuable for planning further studies looking at pain medication reduction in acute and chronic pain management with the InterX 5000 as opposed to a sham.

The patients in this study achieved a sustained response that lasted at least 24 hours in between treatments. This was demonstrated by the numeric pain score reductions of AV, PAS and Illicit pre-treatment on Day 2 as compared to pre-treatment Day 1 of 28%, 19% and 18% respective. On Day 3 as compared to Day 2 the pre-treatment scores of AV, PAS, and Illicit improved by an additional 27%, 27% and 23% respectively. These results indicate that, for most patients, the effects of a 30 minute treatment are sustained for at least 24 hours between treatments. The long term effects and longevity of response need to be further evaluated.

The observations made on three of the patients may indicate possible effects of the InterX 5000 mechanism of action. The improvement of circulation in two of the patients visually, and the effect seen on the "port wine" may indicate autonomic effect on the nervous system. The autonomic effect on the nervous system is thought to be the controlling factor in reflex sympathetic dystrophy which has also been implicated in the chronic pain arch. The InterX 5000 is thought to be effective through over stimulation of the afferent c-fibers. Some of the effect may be mediated through the autonomic nervous system.

While pain numeric scoring is subjective, this pilot study shows subjective improvement of the patients during the three day trial. Statistical treatment of the pilot study will be performed. The pilot study can also serve to define parameters of further studies. This study indicates that the InterX 5000 is a non-invasive, technology that has no known side effects or complications and that the technology may be extremely useful in controlling chronic pain.

Summary

Fifteen orthopedic patients with chronic severe pain demonstrated a large reduction of the pain with the use of the non-invasive InterX 5000 for three days.

Table 1: Patient Histories

Patient Number	Description	Condition
1	76 y/o WF	Status post total knee replacement complicated by a reflex sympathetic dystrophy. After sympathetic blocks patient still complained of tremendous pain and stiffness after manipulation under general anesthetic.
2	44 y/o WM	Status post shoulder disarticulation with complex flaps for treatment of an infected whole prosthetic humerus replacement for osteosarcoma. The patient was almost comatose from "pain" management for neurogenic pain (phantom pain). Surgery was eight weeks earlier.
3	35 y/o WF	Underwent pelvic and abdominal resection of a left iliac wing aggressive fibromatosis necessitating marlex reconstruction of anterior abdominal wall, gluteal advancement flaps and adjacent soft tissue transfer for closure. She had received 5000 CGy locally through electron beam pre-op. Her pain was surgical site pain.
4	36 y/o WF	Underwent resection of a lower leg alteriovenous malformation 18 months earlier. The patient had a persistent port-wine involvement of a hemangioma measuring 10x12 cm^2. The patient course was complicated by a stress fracture after treatment and had persistent lesional pain.
5	46 y/o WM	Underwent resection for aggressive fibromatosisl right scapula. The lesion recurred with intractable pain. The patient received 5280 CGy electron beam irradiation pre-op. The patient had persistent lesional pain.
6	73 y/o WM	Eight months status-post right total knee replacement with a revision prosthesis, necessary for involvement of the distal femur with fibrous dysplasia. The procedure was large and resulted in chronic pain secondary to scarring. Pain was thought secondary to this.
7	63 y/o WF	Metastatic carcinoma of the breast involvement of right ischium. The patient underwent wide resection of pelvic involvement and was reconstructed with pelvic plates and cement and total hip arthroplasty. The patient received radiation prior to surgery and has received pre-op and post-op chemotherapy. The pain was thought secondary to the large surgical procedure.
8	63 y/o WF	Presented with right failed total knee replacement secondary to prosthetic loosening and wear debris. She underwent total knee revision three months earlier with resection of large psuedotumor caused by prosthetic debris. The patient had persistent lymphedema. The pain was thought secondary to the large size of the surgery and lymphedema.

Patient Number	Description	Condition
9	57 y/o WF	Presented with bilateral total knee infections associated with septicemia from an infected cardiac value. The patient has undergone six operations to control her infected knees. She has extensive scarring, lymphedema and circulatory problems to her feet. Her last revisions were three months prior to treatment. Her pain was thought secondary to the large surgeries on both knees and lymphedema.
10	25 y/o WF	Sustained gunshot wound to left hip and right elbow. The patient has undergone numerous treatments on both hip and elbow and upper arms for osteomyelitis resulting in total elbow and partial humerus replacement and pelvic reconstruction. The patient has persistent pain thought secondary to reflex sympathetic dystrophic, neurogenic pain from the gunshot and surgical site pain in hip and elbow.
11	52 y/o WM	Presented with failed total right knee replacement. He underwent a complex revision with excisional scar three months earlier. His persistent pain was thought secondary to the large surgical procedure.
12	52 y/o WF	Presented with failed left total knee replacement. The patient underwent complex revision three months earlier. Her pain was thought secondary to the large surgical procedure.
13	14 y/o WF	Pain following a grafting procedure for fibrous dysplasia of right hip. Her surgery was six months earlier and now has structural defect secondary to recurrence of a cystic bone lesion. Her pain is thought secondary to the lesional recurrence.
14	75 y/o WF	Long-term history of multiple myeloma. The patient underwent total hip replacement 18 months earlier. She has femoral component failure secondary to loosening. The patient is not a surgical candidate for revision because of cardiomyopathy induced by chemotherapy. Her pain is secondary to femoral component loosening.
15	78 y/o WF	Infected total hip and total knee replacements on the left side. The patient has undergone 10 surgical procedures for treatment finishing with total knee, total femur and total hip replacement. The patient has persistent lymphedema. The pain is thought secondary to surgeries in past lymphedema, and reflex sympathetic dystrophy.

Table 2: Day 1 – Numeric Pain Scale Ratings

Patient ID #	Before Treatment			After Treatment		
	AV Pain	PAS	Ilicit	AV Pain	PAS	Ilicit
1	4	6	6	2	2	1.5
2	7	6	6	4.5	6.5	4.5
3	8	8	9	4	0	0
4	10	7	7	4	4	4
5	8	10	10	6	5	7.5
6	8	6	6	0	0	0
7	4	3	3	2	1.5	0
8	2	2	4	0	0	3.5
9	6	6	4	2	2.5	4.5
10	5.5	6	3	0	0	0
11	5	5	5	0	0	2
12	5	4	7	1	1	3.5
13	6	6	6	0	0	1.5
14	4	6	5.5	0	0	0
15	6	6	7.5	5	5	5
16	3	8	8	2	3	3
17	3	5	10	1	2	4
18	5	8	10	5	6	7
19	6	0	10	0	0	0
20	10	10	10	4	4	4
21	8	8	8	4	4	4
22	8	8	8	5	5	5
Average	6.0	6.1	7.0	2.3	2.3	2.9

Table 3: Day 2 – Numeric Pain Scale Ratings

Patient ID #	Before Treatment			After Treatment		
	AV Pain	PAS	Ilicit	AV Pain	PAS	Ilicit
1	2	2	3	0	0	0
2	6	6	6	3	3	3
3	6	6	7	0	0	1.5
4	10	10	10	5	5	5
5	5	1.5	0	3	2.5	2
6	0	0	1	0	0	0
7	3	3		0	0	0
8	0	0	3	0	0	2.5
9	7.5	7.5	8.5	3	3	3
10	3	3	4	0	0	0
11	2	3.5	6.5	0	0	0
12	1	1	4	1	1	1
13	1.5	1.5	1.5	3	3	3
14	6	7	7	1	0	0
15	6.5	6.5	7.5	4.5	4.5	4.5
16	8	8	8	1	2	2
17	4	6	8	2	3	4
18	7	8	10	5	5	6
19	5	8	10	3	4	4
20	4	4	4	1	1	1
21	6	8	9	0	0	2
22	1	8	8	0	6	6
Average	4.3	4.9	5.7	1.6	2.0	2.3

Table 4: Day 3 – Numeric Pain Scale Ratings

Patient ID #	Before Treatment			After Treatment		
	AV Pain	PAS	Ilicit	AV Pain	PAS	Ilicit
1	1	1	1	0	0	0
2	6.5	6.5	6.5	2.5	2.5	2.5
3	5.5	5.5	5.5	0	0	0.5
4	6	6	8	2.5	2.5	4
5	8	9	9	6	7	7
6	0	0	0	0	0	0
7	2	2.5	2.5	0	0	0
8	1	1	7	0	0	4
9	0.5	0.5	0.5	0	0	0
10	0	0	0	0	0	0
11	2	3.5	3.5	0	0	0
12	2	2	2	0	0	0
13	4	4	6	3	3	3
14	2.5	5	6.5	0	0	0
15	5	5	5.5	5	5	5.5
16	0	4	4	0	0	0
17	2	1	3	1	1	2
18	7	7	8	6	6	7
19	7	4	6	0	0	0
20	2	3	3	0	0	1
21	1	3	3	0	0	0
22	4	6	6	0	3	3
Average	3.1	3.6	4.4	1.2	1.4	1.8

Table 5: Overall Change in Numeric Rating Scale

Patients highlighted in red reduced their pain medication during or immediately prior to treatment.

Patient ID #	Overall Change		
	AV	PAS	Ilicit
1	4	6	6
2	4.5	3.5	3.5
3	8	8	8.5
4	7.5	4.5	3
5	2	3	3
6	8	6	6
7	4	3	3
8	2	2	0
9	6	6	4
10	5.5	6	3
11	5	5	5
12	5	4	7
13	3	3	3
14	4	6	5.5
15	1	1	2
16	3	8	8
17	2	4	8
18	-1	2	3
19	6	0	10
20	8	8	7
21	8	8	8
22	8	5	5
Average	4.7	4.6	5.1

Table 6: Medication History

ID #	Before Study (Daily Intake)	Day 1	Day 2	Day 3
1	1 Hydrocodone	None	None	None
2	16 Hydrocodone – 2 each 8 times/day	2 Hydrocodone once daily	Same	Same
3	Voluntarily removed patch 1 day before trial	No medications	No medications	No medications
4	No medication	Same	Same	Same
5	1 Tylenol	Same	Same	Same
6	2 Ultracet	Same	Same	Same
7	1 Advil	Same	None	None
8	1 Hydrocodone	Same	Same	Same
9	2 Hydrocodone once daily	Same	Same	Same
10*	8 Hydrocodone Duragesic Patch	4 Hydrocodone	3 ½ Hydrocodone Patch removed for 8 hours	3 ½ Hydrocodone Patch removed for 8 hours
11	3 Hydrocodone Duragesic Patch	Duragesic Patch	None	None
12	Hydrocodone	Hydrocodone	None	None
13	Duragesic Patch	Duragesic Patch	None	None
14	None	Same	Same	Same
15	2 Norco – 2 times/day 1 Methadone @ PM	Same	2 Norco – 1/day 1 Methadone	No narcotics 1 Methadone

** Patient 10 reduced medication to a level that did not result in withdrawal symptoms. The patient continues to work with her physician to determine the best course on narcotics reduction.*

References:

[1] Coleman, S, *Knee Injuries – InterX Therapy to Solve Unsolved Sports Injuries*, presented at the International Congress on Sports Rehabilitation and Traumatology, Bologna, Italy, 2005.

[2] Neuro Resource Group, Inc., *Clinical Investigation – InterX 5000 Technical File*, 2004.

[3] Neuro Resource Group, Inc., *510(k) Submittal #K042912*, October 20, 2004.

[4] OKB RITM, SCENAR-Expertise, Issue #8 ISBN 5-8327-0011-2, 2002.